VOLUME I—NUMBER 4 APRIL 1950

UNITED STATES ARMED FORCES

MEDICAL JOURNAL

Published monthly by the Department of Defense

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THE PRINTING OF THIS PUBLICATION HAS BEEN APPROVED BY THE DIRECTOR OF THE BUREAU OF THE BUDGET, OCTOBER 19, 1949.

Congestive Heart Failure

Backward and Forward Failure Hypotheses

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ALTHOUGH thousands of patients have been treated for congestive heart failure, there is no universally accepted theory regarding the altered physiologic state in this condition. It would be well to define the conceptions of heart failure, circulatory failure, and congestive heart failure before beginning a general discussion of the subject. Dock (*1*) states:

> Heart failure should be applied only to the clinical disorder which is due to the inability of the myocardium of the ventricles to maintain the requisite flow of blood to all the tissues of the body. Circulatory failure should be used for those conditions in which requisite flow is not maintained in spite of an adequate myocardium because shock, hemorrhage, pericardial tamponade, constrictive pericarditis, or extreme rates of tachycardia prevent adequate diastolic filling of the ventricles.

This indicates that in circulatory failure there is no primary weakness of the myocardium.

The term, "congestive heart failure," is applied to that syndrome in which myocardial weakness is associated with such signs and symptoms as edema, increased blood volume, increased venous pressure, and the concomitant symptoms of dyspnea and weakness. In short, con-

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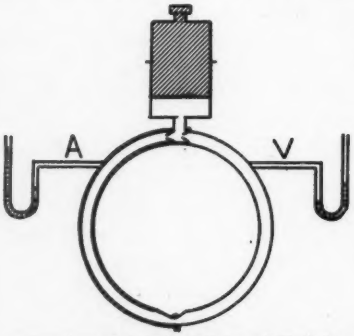
gestive heart failure is waterlogging of the tissues in close association with myocardial weakness.

MECHANISM

How does this occur? In 1832, James Hope propounded the "dam and stream" analogy (*2*) (*3*). This is the basis for the so-called "backward failure" theory of congestive failure (*4*). The "dam and stream" analogy pictures the blood in the great veins as being a pond before a dam in a flowing stream. The heart is the pump which lifts the water over the dam. As the pump weakens more water runs into the pond than is pumped out, and the water level (venous pressure) rises (*2*). In other words, blood backs up behind the failing heart.

In 1889, Julius Cohnheim made the first studies on experimentally produced heart failure by injecting oil into the pericardial cavities of animals, producing pericardial tamponade. This not only gave rise to an increase in venous pressure, but also a fall in arterial pressure. Hence, he concluded that inadequate cardiac output, so-called "forward failure," played a part in the clinical syndrome as well as the "backward failure" (*5*). It should be noted that Cohnheim actually produced circulatory failure, according to the definition as stated before, and not congestive heart failure as we ordinarily think of it.

In the late nineteenth century the development of apparatus for the experimental study of circulatory phenomena came into vogue (*2*). One of the simplest forms of circulation schema is shown in figure 1 (after Starr) (*2*). The apparatus works as follows. Before the pump is started a pressure of 10 mm. exists throughout the system. This is the static pressure. When one pumps hard the pressures become: A=120, V=4. When one pumps weakly, the pressures become: A=70, V=8. Increasing the resistance at the pinchcock increases arterial pressure but always diminishes venous pressure simultaneously; decreasing resistance has the opposite effect. Increased venous pressure together with a maintained arterial pressure cannot be brought about by either weakening the pump, changing the resistance, or any combination of the two. Let us now inject more water into the system. This lodges chiefly in the most distensible parts, that is, the "veins." The static pressure is now 20 mm. After beginning to pump, A=120, V=15. Increased venous pressure in the presence of a normal arterial pressure is now attained.



—Courtesy of Annals of Internal Medicine.
Figure 1.—The simplest form of circulation schema.

About 35 years ago Starling and his associates published their work with the heart-lung preparation, from which the "law of the heart" was formulated. In brief, Starling's law states that the energy output of the heart is directly related to its diastolic volume (*6*).

All of the foregoing work has formed the basis for the "backward failure" theory, which has been so widely accepted that Starr (*2*) speaks of it as the "classical" view. It may be well at this time to state in simple terms this classic view of "backward failure." Overwork of the heart leads to enlargement, particularly of those portions of the heart which are subjected to the increase in work. If dilatation of a chamber becomes extreme, there is a rise in the venous pressure behind the chamber. This increased venous pressure leads to congestion of the organs drained by these veins. For example, in a patient with mitral stenosis, dilatation of the left auricle eventually occurs. Subsequently, increased pulmonary venous pressure and pulmonary congestion occur, followed by an increase in the pulmonary arterial pressure with consequent strain upon the right ventricle. Continuing with this line of reasoning, the right ventricle dilates, the tricuspid valve becomes incompetent, and the venous pressure in the right auricle and systemic veins is elevated. It is the increased venous pressure in the peripheral circulation that theoretically brings about the congestion and peripheral edema so characteristic of congestive heart failure.

This classical view has been accepted by most French and German clinicians since Hope's day (*4*). It has been clearly expressed and the conception of left and right heart failure has been carefully delineated by Harrison (*5*). He concludes that the clinical manifestations of congestive heart failure are due to back pressure, dyspnea being brought about by pulmonary congestion which is the result of back pressure from the left side of the heart. The peripheral edema follows congestion of the systemic circulation which is dependent on the back pressure from the right side of the heart. In both instances, the rise in venous pressure is dependent on dilatation of the chambers of the corresponding side of the heart, the dilatation being a manifestation of fatigue of the cardiac muscle. The dilated heart is an inefficient pump for, although it may supply an adequate amount of blood, it expends excess energy in carrying on this work. Heart failure should be attributed in the main to inefficiency, rather than to insufficiency, of the myocardium (*5*).

In the English-speaking countries, until recently, the most favored theory has been the "forward failure" of Ellis (*4*) ("recently" coinciding with Harrison's (*5*) views). In simple terms, the "forward failure" theory holds that the manifestations of cardiac decompensation are caused in the main by an inadequate output of blood by

the heart (*4*). In other words, the function of the heart is to pump blood to meet the metabolic requirements of the body; thus the symptoms of the failing heart are primarily caused by an inadequate cardiac output and not to an increase in venous pressure behind the failing cardiac chamber. The "forward failure" theory was advocated by Sir James MacKenzie, Sir Thomas Lewis (*4*), and many others. It was with the advent of the work of the Stead group (*7*) in 1944 that this theory again gained popularity. Stead observed that many patients showed an increase in extracellular fluid, i. e., an increase in weight, before they showed an increase in venous pressure. In other words, there is a retention of salt and water prior to the development of the increased venous pressure, which is supposedly the first phenomenon associated with cardiac failure according to the backward pressure theory.

Before entering into a more detailed discussion of the chain of events which purportedly occurs according to these two main hypotheses, we should briefly review the physiology of edema formation, blood volume regulation, changes in venous pressure, and the regulation of cardiac output by examining their relationship to congestive heart failure.

CHARACTERISTICS

Edema is a prominent sign associated with progressive heart failure. Fluid transfer between the capillaries and the extracellular spaces depends, in the main, upon the hydrostatic blood pressure, the plasma osmotic pressure, the tissue osmotic pressure and the tissue tension (*8*). Normally, the hydrostatic pressure and the plasma osmotic pressure are the most important factors (*8*). Edema may be caused by: (*a*) increased capillary permeability, as in burns; (*b*) increased hydrostatic pressure (hydrostatic pressure may be augmented by increased venous pressure or arteriolar dilatation); (*c*) lymphatic obstruction; (d) hypoproteinemia; and (*e*) a disturbance of electrolyte and water balance as in Addison's disease. Lymphatic obstruction and increased capillary permeability play little part in the edema of congestive heart failure. The protein content of the edema fluid in congestive heart failure is usually less than 0.5 gm. per 100 cc. (*7*). The protein content of lymphatic edema or transudation due to increased capillary permeability is much higher than this. It should be noted that if anoxemia causes excessive capillary permeability, this mechanism would not appear to be significant in congestive heart failure (*7*).

The other three causes of edema are probably operative in congestive heart failure. The capillary hydrostatic pressure may be raised by increased venous pressure and blood volume. Hypoproteinemia may also be a factor in cardiac edema as the total blood protein concentra-

tion is usually decreased in congestive heart failure for perhaps a variety of reasons, such as hemodilution, decreased protein intake, and increased protein loss (*7*). There is, however, not enough decrease in the total protein concentration on the whole to make this the primary cause of cardiac edema. That there is a decrease in the elimination of salt and fluid by the kidney in congestive heart failure is well known. This retention of salt is thought by Stead and his associates to be the primary factor in cardiac edema. Clinically, the earliest sign of edema formation is a gain in weight, several pounds of fluid may collect in the extracellular areas before a pitting edema is demonstrable.

It is agreed that there is an increased blood volume in congestive heart failure (*5*). This is principally an increase in plasma volume. In the normal resting subject with constant arterial pressure and circulating red blood cells, the plasma volume may be altered by: (*a*) changing the amount of circulating protein; (*b*) changing the capillary hydrostatic pressure; and (*c*) changing the extracellular fluid volume. The first two causes are easily understood. The mechanism of the third cause should be explained. If one decreases the extracellular volume by dehydration, there is also a decrease in plasma volume. Conversely, if the extracellular volume is increased by the use of desoxycorticosterone acetate, the plasma volume increases. Perhaps the best example is seen in nephrosis. Despite the extremely low plasma proteins in nephrosis, the circulating blood volume is maintained by the tremendous increase in extracellular volume, or edema (*7*). In congestive heart failure the extracellular volume and the plasma volume increase and decrease concordantly (*7*).

An increased venous pressure is characteristic of congestive heart failure. It may be brought about by: (*a*) obstruction to the veins; (*b*) vasoconstriction, as by adrenalin, paradrenal sulfate, or angiotonin (*7*); (*c*) gravity (this point is self-evident, but it should be remembered that venous pressure changes due to gravity are much greater than those caused by congestive heart failure); and (*d*) increase in blood volume.

Obstruction to a vein and the effects of gravity are of great importance in the localization of edema but would not of themselves be a common cause of generalized edema. Gravity causes a dependent type of edema in the cardiac patient and a periorbital edema in the nephritic patient. If an edematous nephritic patient is placed in a cardiac position, his edema becomes dependent. As Starr (*2*) states, cardiac patients with edema but without orthopnea may have periorbital edema.

The expanded blood volume plays a part in the increased venous pressure in congestive heart failure, but the role of vasoconstriction

is unknown (*2*). The volume of blood in the great veins can be increased without increasing the total circulating blood volume. This may be brought about by a redistribution of the blood from the arteries and the small vessels as by arteriolar dilatation (decreased peripheral resistance) or by increasing the tissue tension (*2*). The venous pressure may also be elevated as a part of a widespread general vasoconstriction as may be produced in animal experiments by asphyxia (*9*). These latter factors may play a part in the increased venous pressure of congestive heart failure.

It should be noted that all of the preceding factors influencing the venous pressure may be noncardiac in origin.

The relationship of the cardiac output to congestive heart failure can be noted by studying one of the simplest forms of circulation schema (fig. 1).

In general, patients in congestive heart failure have a diminished cardiac output (*7*) (*10*). However, exceptions to this (such as Graves disease, beriberi, arteriovenous fistula, Paget's disease) are well known (*1*). In the circulation schema, if one pumps vigorously the cardiac output and arterial pressure will rise but the venous pressure will fall. If one pumps weakly the converse becomes true. By changing the peripheral resistance the arterial and venous pressures may be changed, but never concordantly (*2*). The only manner in which the arterial pressure and venous pressure can both be raised simultaneously is by the injection of more fluid into the system. This additional fluid naturally goes to the most distensible portions of the system—that is, the veins—and the over-all static pressure is increased. Static pressure is that which exists throughout any circulatory system when the pump is not working. After the static pressure has been increased by the injection of additional fluid, the arterial pressure rises, but the venous pressure falls when the pump is started (*2*). However, the venous pressure is still higher than it was before the addition of the extra fluid.

Stead, Warren, and Brannon (*11*) studied the cardiac output in patients at rest with congestive heart failure. They found the following combinations to exist:

(*a*) Cardiac output low with failure, remains low with the disappearance of symptoms. Symptoms relieved by sodium restriction and continued use of diuretics.

(*b*) Cardiac output low with failure, increases with compensation.

(*c*) Cardiac output normal with failure, remains normal with compensation. Decompensation develops with increased activity.

(*d*) Cardiac output high with failure, falls with compensation. This combination may be shown by restless, apprehensive dyspneic patients whose output is adequate for rest but inadequate with mild

exertion, or by patients with hyperthyroidism, anemia, arteriovenous fistula, patent ductus arteriosis, beriberi, and certain infections (*11*).

From the foregoing it is seen that the degree of cardiac output has no direct relationship to the degree of congestive heart failure, and that the venous pressure is no reliable index of cardiac strength or weakness (*2*).

THE "BACKWARD FAILURE" HYPOTHESIS

The "backward failure" theory states that increased venous pressure is the first sign of myocardial failure and that increase in blood volume, edema, and renal retention of salt and water all follow the increase in venous pressure. It seems reasonable to believe that as the heart fails and dilates, and residual ventricular blood accumulates, there will be a slight increase in central venous pressure (*12*). However, it is quite doubtful that this elevation of central venous pressure is of sufficient magnitude to account for the other characteristics of congestive failure. Altschule (*13*) (*14*) quotes Smirk as stating that the venous pressure commonly found in cardiac decompensation is not in itself sufficient to produce pitting edema. Further, if the initial increase in venous pressure is the cause of cardiac edema, then we would expect the blood volume to decrease as the shift of fluids to the tissues takes place; actually the blood volume is increased. It has been suggested that a high venous pressure causes kidney dysfunction resulting in edema, but raising the venous pressure to the degree seen in early congestive failure, does not decrease the renal blood flow or inhibit excretion of salt and water (*12*). In any case, if this sequence of events is correct, then it should be possible to experimentally produce a rise in venous pressure by damage to the heart. The only way the pressure pattern found in clinical congestive failure can be reproduced in the circulation schema is by increasing the fluid volume.

Starr (*2*) sums up this type of work in experimental animals as follows:

> Increased venous pressure at rest may be caused by constriction of the blood vessels and by increased blood volume, even though the heart is organically sound; and it follows cardiac tamponade, as it must if the heart is to be filled at all. But direct damage to the heart muscle of an intact animal does not cause it as long as the animal is at rest, and therefore increased venous pressure at rest is not the direct consequence of cardiac weakness.

Clinically, the most common example of severe myocardial damage infrequently attended by increased venous pressure or congestive heart failure is myocardial infarction. Yet we hesitate to give intravenous fluids in coronary occlusion for fear of precipitating heart failure. This is a clinical example of the necessity of having an extracardiac

factor present, i. e., increased blood volume associated with a weak heart before congestive failure can occur. If increased venous pressure is the initial sign of a damaged myocardium, it should appear more frequently in myocardial infarction than it apparently does. Dock (*1*) points out that in young vigorous men the normal blood volume is relatively large, and it is in this group that we may see sudden failure following myocardial infarction; whereas in older patients with relatively small blood volumes this does not occur so frequently.

If increased venous pressure is the primary cause of pulmonary edema, then clinically we would expect to see such edema most frequently in that group of patients having the highest venous pressure in the pulmonary circuit. However, as Dock points out in mitral stenosis one frequently observes that the lungs may be free of râles even after right heart failure has set in and the liver is enlarged. We know that these cases of mitral stenosis have been walking about for years with extremely high pulmonary pressures. In animal experiments, Visscher (*12*) was unable to produce pulmonary edema by obstructing the pulmonary veins. Perhaps increased vascular thickening or increased lymph flow plays a part in decreasing the formation of pulmonary edema in mitral heart disease.

Warren et al. (*7*) performed a very simple clinical experiment in order to determine whether the venous pressure was the initial feature in the chain of events following a failing heart. They first treated congestive heart failure patients with bed rest, low sodium diet, and mercurial diuretics. After the patients were controlled, bed rest was continued but mercurial diuretics were withheld. Then a high sodium diet was administered, and frequent observations of weight, blood volume, and venous pressures were recorded. They found a definite increase in weight and blood volume prior to a rise in venous pressure. Starr (*2*) has noted this series of events, also.

Therefore, if a rise in venous pressure is not the primary manifestation of the failing heart, we must look elsewhere than the "backward failure" theory for an explanation of the mechanism for congestive heart failure.

THE "FORWARD FAILURE" THEORY

At the present time the chain of events as expressed by Starr and similarly by Stead et al. to explain the mechanism of "forward failure" is essentially as follows: Impaired cardiac function, retention of salt and water; increased blood volume; and then venous congestion. In association with this chain of events there is hemodilution, and both a decreased hematocrit, and decreased percentage of circulating proteins. Merrill (*15*) has shown that the renal blood flow in the presence of congestive heart failure is greatly reduced and that the filtra-

tion rate is also reduced. He has reported that the retention of salt by the kidney resulting in the edema of congestive heart failure is caused by a low filtration rate and not by an increased reabsorption of salt. The renal blood flow was found to be reduced to about one-fifth of normal when the cardiac output was reduced only to about one-half of normal, indicating a specific diversion of blood from the kidney. Merrill believed that when the cardiac output became inadequate to meet the metabolic demands of the body ("forward failure") the blood may be diverted from the kidneys to other parts of the body having greater metabolic needs. He further found that there was no correlation between renal blood flow and venous blood pressure. The mechanism of congestive failure may be explained as follows:

(*a*) *Heart disease.*—Myocardial dysfunction is the most common denominator of congestive heart failure.

(*b*) *Renal retention of salt and water.*—If heart disease is progressive, a time will come when the cardiac output is insufficient to meet the demands of the body. This inadequacy, everything else being equal, would be most likely to occur first under excessive metabolic demands, i. e., the signs of the slowly failing heart should first become apparent on exercise anemia, severe infection, or other complications. The cardiac output would thus be adequate for the body at rest but inadequate under excessive metabolic demands. Clinically, such a situation certainly appears to exist, for many patients, if not most, will compensate on bed rest alone unless the heart disease is rapidly progressive.

If the cardiac output is insufficient to meet the metabolic demands of the body, what homeostatic compensatory mechanisms are available to aid in the adjustment of the inadequate heart? The blood circulation may be augmented by speeding the rate, as in anemia or beriberi, or by increasing the total blood volume. In situations in which the circulatory rate is primarily increased the failure that develops is of high output type; with compensation the cardiac output falls. The clinical examples of increased metabolism in which the total blood volume is increased apparently as a compensatory mechanism, occurs in hyperthyroidism, and in pregnancy where the metabolic demand must be high. Perhaps it is this compensatory mechanism which develops in cases of congenital heart disease. A compensatory blood volume increase also occurs in the polycythemia of high altitudes. If the cardiac output is inadequate the body may compensate by increasing the circulating medium.

Dock (*1*) states:

> When decrease in cardiac output is due to shock or hemorrhage, the immediate effect of changes in the tone of venules and arterioles is to bring venous pressure back toward normal, and to shift the balance of fluid change between blood and

tissues towards the intravascular side. Thus blood volume tends to increase by hemodilution unless the patient is dehydrated.

This temporary mechanism in shock is not sufficient to explain the blood volume changes in congestive heart failure. Obviously, if salt and water were retained by the kidneys, the blood volume would be increased, and certainly in congestive heart failure urinary excretion is decreased. As a part of the compensatory mechanism to maintain or expand the blood volume the kidney may reabsorb sodium. It is axiomatic that if either sodium or chloride or water is retained primarily, the others will be retained to maintain electrolyte balance (*7*). Peters (*16*) states that the kidney manages salt and water excretion or retention in the following manner: As approximately 180 liters of isotonic glomerular filtrate pass through the proximal tubules per day, 60 to 80 percent of the water, all the glucose and fractions of other solutes are removed, together with a quantity of sodium and chloride. A hypotonic solution is left, but the sodium to chloride ratio, previously about 1:3, is now 1:1—as the sodium bicarbonate has been reabsorbed leaving the remaining sodium as sodium chloride. In the loop of Henle a variable amount of sodium chloride is withdrawn with some water; however, more salt than water is reabsorbed here, leaving a hypotonic solution. Finally, in the terminal convoluted tubule water is absorbed to yield the fully elaborated urine which is usually hypertonic. The renal reabsorption of water in the terminal tubule appears to be chiefly controlled by the antidiuretic hormone of the posterior pituitary. However, in the presence of an excess amount of salt this hormone will not cause an increased reabsorption of water. In other words, the salt demands water for excretion and has a functional or osmotic priority for water over the hormone. Therefore, when the body needs to retain fluid it must retain salt, for the terminal tubules, although stimulated by the posterior pituitary, cannot reabsorb water in the presence of excess salt. Thus, as a compensatory mechanism to expand the blood volume we would expect the kidneys to reabsorb sodium first and water secondarily. It is believed that part of the mechanism of sodium reabsorption is governed by the adrenal cortex, although other factors are probably operative, such as the enzyme system in the distal renal tubular cells. That sodium is the important factor is demonstrated by the action of mercurial diuretics. Reaser and Burch (*17*), using radioactive Na^{22}, demonstrated that in a mercurial diuresis the excretion of sodium preceded the water diuresis by 2 to 4 hours. Regardless of whether the retention of salt and water is caused primarily by decreased renal blood flow or to hormonal or enzyme factors, the important point is that a renal mechanism exists through which compensatory changes in blood volume may be made.

(*c*) *Increased blood volume* follows renal retention of salt and water.

(*d*) *Edema formation.*—As a result of increased blood volume there is an increase in hydrostatic pressure. (Starr (*2*) demonstrated an increase in hydrostatic pressure by measuring the venous pressure after death in patients who had succumbed to congestive heart failure.) With the increase in hydrostatic pressure transudation of fluid would occur.

(*e*) *Increased venous pressure.*—With the increased blood volume and increased tissue tension due to edema, two of the main causes of increased venous pressure would be present. Venous congestion would thus result. As the blood volume and extracellular fluid vary concordantly in congestive failure, the more edema present the greater the increase in blood volume and the greater the increase in venous pressure.

(*f*) *Increased work of the heart.*—According to Starling's law, the greater the venous pressure and diastolic filling of the heart, the greater the cardiac output. Hence, all of the foregoing events, from the renal retention of salt and water to the increase in venous pressure, are compensatory mechanisms which augment the cardiac output necessary for the adequate blood supply of the body. However, as Starling demonstrated, the metabolism of the myocardium is directly proportional to the diastolic volume (*6*). This increased metabolic need of the heart would lead, in the presence of progressive myocardial disease, to additional heart damage.

(*g*) *Additional heart damage.*—With progressive myocardial disease the foregoing series of events would be compounded and eventual, irreversible congestive heart failure would occur.

As an example, let us apply the preceding chain of events to cases of hypertensive heart disease with beginning failure of the left ventricle. The first signs of failure should occur with an increase in the basal metabolic rate. Many hypertensive patients can be up and about all day with little difficulty until they assume the decubitus position at night. However, because of inadequate output during the day, renal blood flow and sodium excretion are decreased, and the compensatory increase in blood volume occurs. Dock (*1*) states that these changes occur in normal subjects when kept in the upright position, which in itself reduces cardiac output by trapping blood in the distended veins below the diaphragm. Thus in these patients there is an increased blood volume which they do not need when they retire at night, for the cardiac output is then adequate to meet the basal metabolism during sleep. There is a consequent shift of intravascular fluid to extravascular areas, localization to the pulmonary circulation being favored by the tremendous pulmonary capillary bed and gravity.

There is a normal shift of venous blood to the thorax on assuming the recumbent position. This accounts for the reduction in vital capacity of approximately 8 percent found in normal persons when they lie down (*5*). In orthopneic congestive heart-failure patients the vital capacity is reduced an average of 25 percent by this position.

In addition, there are factors that probably favor increased right ventricular and lessened left ventricular output. During inspiration the output of the right heart is relatively greater than the output of the left heart (*6*). Further, it is recognized that inspiration is an active process and expiration a passive process, the latter being therefore greatly influenced by gravity and position. It is possible that in the recumbent position the right ventricular output tends to be relatively greater than the left.

Cournand states:

> The volume of blood contained in the pulmonary vessels is governed by the relative discharge of the two sides of the heart which are under the control of the dynamic changes in the systemic circulation.

Also,

> The capacity and the flexibility of the small vessels in the lungs are such that a several-fold increase in blood flow may be accommodated with negligible pressure changes.

When the hypertensive patient with left ventricular failure lies down, because of his increased blood volume the previously mentioned factors cause an abnormally large shift of fluid to the pulmonary circuit. As a large amount of fluid can be retained in the lesser circulation before a rise in pressure occurs, one may postulate that sudden pulmonary edema would ensue in the presence of a reduced vital capacity before an increased pulmonary venous pressure would bring about a compensatory left ventricular output. That this mechanism of paroxysmal nocturnal dyspnea is correct is supported by the fact that usually the patient gains immediate relief from the symptoms by merely sitting up and breathing deeply. In so doing he increases his vital capacity and cardiac output. Patients with mitral stenosis seldom undergo this sudden nocturnal pulmonary edema because their pulmonary pressure is already elevated, and pronounced differences of cardiac output are not produced in such an abrupt fashion (*6*).

From the foregoing discussion of congestive heart failure it is apparent that the compensatory increase in blood volume is a long-term adaptation phenomenon which, although useful to a point, becomes deleterious in the end (*12*). Dock (*1*) gives the background of this compensatory mechanism as follows:

> The rise in arterial pressure in heart failure and all the classical features of congestive failure are due to the fact that mammals have developed a complex and effective mechanism for dealing with a decrease in cardiac output occurring

in shock, hemorrhage, and dehydration, and that this mechanism comes into play whenever the cardiac output is reduced for any reason whatever. Without such a mechanism, heart failure would result only in fatigability, or if severe, in anuria and abdominal distention, weakness and syncope. The mammal evolved no reflex mechanism for dealing with myocardial failure as such, for the obvious reason that wild animals do not have heart failure during the normal reproductive life span. In civilized man the development of congestive failure is hastened by the high salt content of the diet, which makes possible rapid increases in blood and intercellular fluid volume, and by alternation between an erect posture, which diminishes cardiac output, and recumbency, which allows blood and edema fluid in the legs to be mobilized and pile up in the lungs.

SUMMARY

The chain of events in the "forward failure" theory of heart disease may be outlined as follows: inadequate cardiac output, renal retention of salt and water, compensatory increase in blood volume, edema, elevation of venous pressure, increased ventricular diastolic volume, and temporarily increased cardiac output. In the presence of progressive myocardial disease, eventual, irreversible failure.

It is believed that the basic mechanism of chronic congestive heart failure is most compatible with the hypothesis of "forward failure." The "backward failure" features, although certainly operative to some degree, are not primary. A proper conception of the pathogenesis of this syndrome is necessary, for although little can be done for the cardiac factors involved, much may be done for the noncardiac factors, such as retention of salt and water and compensatory increase in blood volume. As Starr (*2*) points out, "factors directed to the elimination of fluid are becoming more and more successful in handling these cases and we are only at the beginning of our knowledge of this subject."

Clinically we are now seeing an increasing number of patients in whom, because of the restriction of salt and the use of mercurial diuretics, the classical signs of congestion and edema in the presence of an inadequate cardiac output are held in abeyance. In this group of patients the paramount limiting factors on activity are weakness and fatigue (*14*).

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COMPARISON OF DIFFERENT REGIMENS IN THE TREATMENT OF HEPATIC CIRRHOSIS, by Gordon R. Morey, M. D., and Robert M. Kark, M. D. Journal of Laboratory and Clinical Medicine 34: 1727–1728, Dec. 1949.

Clinical, laboratory, and metabolic observations were made on patients with hepatic cirrhosis during treatment with different therapeutic regimens. All of the patients improved on a diet which contained (*a*) calories equivalent to twice the calculated basal requirement; (*b*) 2.5 gm. of protein per kilogram of body weight; and (*c*) 30 percent of the calories as fat. The patients' clinical improvement was accelerated by daily intravenous infusions of a mixed amino-acid solution which was sodium-free. Restriction of the sodium intake below 1 gm. per diem was a valuable adjuvant in combatting fluid retention. No clinical benefits were observed when the basic regimen was supplemented with cystine, methionine, choline, B complex vitamins, or parenteral liver extract. The infusion of large amounts of serum albumin was impractical as a method of protein supplementation even though a transient rise in serum albumin concentration and an increase in positive nitrogen balance attended its administration. On diet, salt restriction, and supplementation with amino-acid infusions all of the patients showed weight gains without fluid retention.—*Abstract.*

Obesity as a Problem in Preventive Medicine[1]

WELDON J. WALKER, *Lieutenant Colonel, MC, U. S. A.*[2]

THE greatest problem in preventive medicine in the United States today is obesity. It has exceeded the combined total of the four next most common causes for rejection on medical grounds of applicants for standard life insurance (*1*). Table 1 shows the ideal height and weight for men and women. These weights approximate the average found in adults of medium frame between 25 and 30 years of age. To obtain ideal weights for persons with small frames subtract 5 percent and for those with large frames add 5 percent. This table makes no age distinction for adult groups because those tables that indicate progressively increasing weight with advancing years merely reflect the increasing incidence of obesity with age. As a matter of fact, there is a progressive diminution of muscle mass after the age of 25 years (*2*). The body weight should, therefore, be less at 50 than at 25 years.

TABLE 1.—*Ideal weights for height for adults of medium frame*[1]

Height (with shoes)	Weight in pounds (as ordinarily dressed)	
	Men	Women
5 feet	----	116
5 feet 1 inch	----	118
5 feet 2 inches	129	121
5 feet 3 inches	132	124
5 feet 4 inches	135	128
5 feet 5 inches	139	131
5 feet 6 inches	142	135
5 feet 7 inches	146	139
5 feet 8 inches	150	142
5 feet 9 inches	155	146
5 feet 10 inches	158	150
5 feet 11 inches	162	153
6 feet	167	157
6 feet 1 inch	172	----
6 feet 2 inches	178	----
6 feet 3 inches	183	----

[1] After "Ideal Weights for Men," Statistical Bulletin, Metropolitan Life Insurance Company, 24: 6-8, June 1943; and "Ideal Weights for Women," Statistical Bulletin, Metropolitan Life Insurance Company, 23: 6-8, Oct. 1942.

[1] Read before the Medical Association of the Isthmian Canal Zone, 18 January 1949.

[2] Gorgas Hospital, Ancon, C. Z.

Tables 2 and 3, and figure 1 show that excess weight is a health hazard that carries a much greater risk in persons beyond 45 years of age than in younger persons. In fact an excess of 50 pounds at 45 increases mortality as much as valvular heart disease (*3*). The most favorable weight at this age is appreciably below that given in the standard tables. The preceding comparisons, unfavorable as they are to overweight persons, are based on the best of the group, namely life insurance policyholders, who had been selected by medical examination as free from any other serious physical impairment. If all overweight persons were included, their decreased longevity would be even more pronounced.

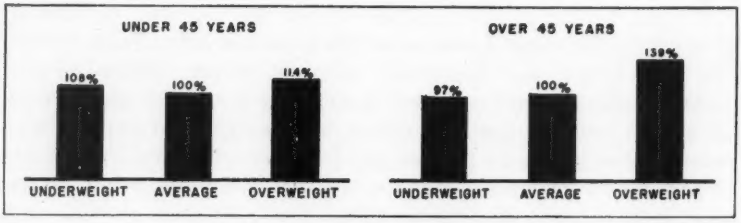

Figure 1.—Influence of weight on mortality as modified by age. (Adapted from (Newburgh (18).)

TABLE 2.—*Influence of weight on mortality in insured persons* [1]

Weight	Deaths per 100,000	Percent of standard
Standard	844	100
Underweight, total	848	101
Overweight, total	1,111	132
Underweight, 5–14 percent	833	99
Underweight, 15–34 percent	913	108
Overweight, 5–14 percent	1,027	122
Overweight, 15–24 percent	1,215	144
Overweight, 25 percent or more	1,472	174

[1] After "Length of Life," by Dublin and Lotka, (*14*).

TABLE 3.—*Influence of overweight on mortality in persons aged 45 to 50 years* [1]

Overweight:	*Increased mortality (above average) percent*
10 pounds	8
20 pounds	18
30 pounds	28
40 pounds	45
50 pounds	56
60 pounds	67
70 pounds	81
80 pounds	116

[1] From "Obesity" by Newburgh, (18).

There are numerous diseases that show an increased mortality in overweight persons. These are chiefly the chronic degenerative diseases. Figure 2 shows the influence of weight on the mortality from cardiovascular renal disease. Insurance studies have shown sustained hypertension to occur more than three times as often in overweight persons as in others (*4*). A recent study involving 22,741 Army officers covering a 10-year period showed 2.5 times the incidence of hypertension in the overweight group (*5*). An even more startling correlation is seen between obesity and diabetes (fig. 3). Americans are not only the best fed people in the world, but they also have the highest death rate from diabetes of any country (*6*). At present there are about 2 million diabetics in the United States (*7*). It is estimated that one-half could be removed from this roll by weight reduction (*8*). If the present trend continues 3,873,000 persons who are living in 1940 either have or will develop the disease (*9*). Between 1900 and 1943 diabetes rose from twenty-seventh to eighth place as the primary cause of death in the United States despite the discovery of insulin (*10*). There is also a greater incidence of cancer in the obese person (*11*). The mortality from surgical procedures is higher in the overweight. Deaths from accidents are more frequent—when the fat man falls he falls harder. The incidence of biliary tract disease, joint disease, intertrigo, varicose veins, and hernia is also increased. The greater number of suicides does not agree with the common belief that the fat man is by nature jolly (*14*).

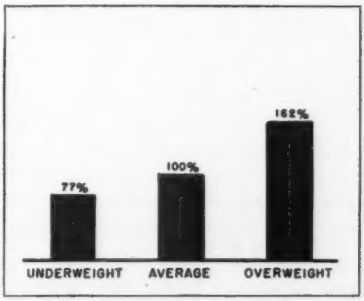

Figure 2.—Influence of weight on mortality from cardiovascular renal disease. (Adapted from Dublin and Lotka (12).)

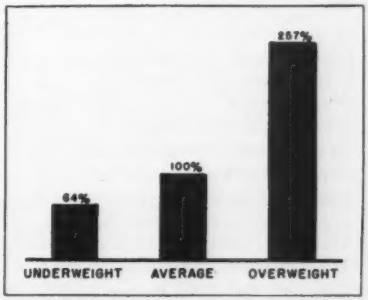

Figure 3.—Influence of weight on mortality from diabetes. (Adapted from Dublin and Lotka (12).)

Incidence of obesity.—In one study 2.1 percent of the men and 4 percent of the women applying for life insurance were rejected for any insurance for this reason (*12*). In a study of insurance policyholders, obesity was defined as more than 20 percent above the average weight. Under 25 years of age the incidence was 4.9 percent with

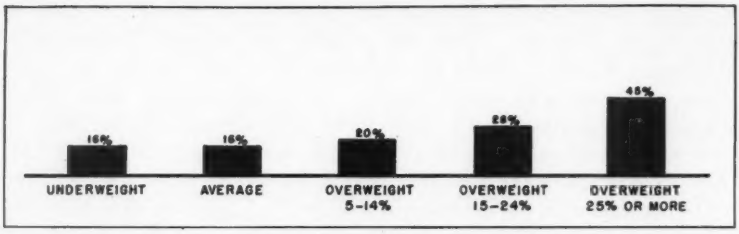

Figure 4.—Relation of weight to hypertension in 594 employees of the Panama Canal. (Hypertension considered to be blood pressure of 140/90 or above.)

a progressive increase to 19.8 percent at age 55 (*13*). The incidence in persons over 60 years of age dropped off presumably because few obese persons live beyond that age (*14*). In January 1949, 594 male employees of the Panama Canal received their annual physical examination. The incidence of overweight found is shown in table 4. The incidence of obesity in this group increased, progressively with age, from 7 percent between 21 and 24 years to 28 percent between 55 and 62 years. The correlation between increased weight and elevated blood pressure is shown in figure 4. Although single elevated blood pressure readings are found in many persons who do not have sustained hypertension the importance of transient hypertension as a forerunner of sustained hypertension is well known and this study demonstrates a significant increase of elevated blood pressure with increasing weight.

TABLE 4.—*Weight distribution of 594 employees of the Panama Canal*[1]

15–24 percent underweight	10
5–14 percent underweight	67
Plus or minus 5 percent of the average weight	159
5–14 percent overweight	154
15–24 percent overweight	125
25 percent or more overweight	79
Percent of employees overweight	60
Percent of obese employees[2]	22
Average number of pounds overweight in overweight group	28
Average number of pounds overweight in obese group[2]	44
Expected increased mortality in overweight group	26
Expected increased mortality in obese group	50

[1] Ages ranged from 21 to 62 years. 55 percent were 45 years old or older.
[2] Persons more than 20 percent above the average weight.

Cause of obesity.—Although studies published 25 years ago pointed out the high mortality associated with obesity there was little medical interest in the subject largely because of the widespread belief that obese persons had some ill-defined glandular or metabolic disturb-

ance that caused them to be fat, regardless of what they ate (*3*). Recent studies, particularly those by Evans (*2*) and Newburgh (*8*), have established the fallacy of such beliefs. Obesity always results from the ingestion of more calories than are expended. Many obese persons state that they eat little or nothing and continue to gain. Their intake may be small in volume but not in calories. Evans (*2*) hospitalized a group of such patients and instructed them to continue to eat as they did at home. Their intake averaged 2,570 calories per day, and yet there was an average weight loss of 2 pounds in 4 days.

The term endocrine obesity is inaccurate. Obesity may occur in association with endocrine disease and is produced in the same way as any other obesity. Although it is known that hypothyroidism is characterized by impaired absorption of food from the intestines and that myxedematous patients are not generally obese, the idea persists that hypothyroidism is a cause of obesity (*15*). Plummer (*16*) studied 200 persons suffering from various grades of myxedema and found 61 percent were overweight. The greatest excess weight corresponded, however, to the least depression of metabolism, and those patients whose basal metabolic rates were lowest weighed the least. A few days treatment with thyroid extract resulted in diuresis with loss of edema after which their group weight was less than normal. A certain percentage of fat persons and an equal percentage of slender persons will show basal metabolic rates in the range of -10 to -30. Unless there is an associated reduction of organic blood iodide, this probably represents their normal metabolic level and is not an indication for thyroid hormone therapy (*17*). To attribute obesity to hypofunction of the anterior pituitary is hard to rationalize in view of the severe cachexia that results from destruction of this gland. The buffalo hump and protuberant abdomen of adrenal cortical hyperfunction have been shown to be totally unrelated to adiposity, and to result from demineralization with shortening of the vertebral column (*18*).

Although lesions in the hypothalamus of experimental animals result in increased appetite that leads to adiposity (*19*), in man a positive correlation between obesity and lesions of the hypothalamus has not been established (*21*). It has also been claimed that fat persons digest and absorb their food with greater than normal efficiency. Such claims have been refuted (*22*).

The causes of obesity, therefore, are those factors that lead to excessive caloric intake. Overeating is largely a habit, both as to the amount and type of food eaten. This seems to be the largest factor in the familial incidence of adiposity. In one study patients who were given a bulky diet containing one calory per gram lost weight

(*24*). When given a diet containing 2.5 calories per gram all gained weight. This suggests that we become accustomed to a habitual volume of food. The importance of psychologic factors in obesity is gaining recognition. Menopausal obesity is probably a manifestation of increased leisure and boredom as well as increased nervous tension. Many persons grow fat because life has become more difficult for them and they obtain temporary solace in eating; like the alcoholic who drinks because life is too hard. In a study of 200 obese persons, Freed (*25*) found that 40 percent had enuresis as children and a high incidence of delayed emotional maturity. Any type of nervous tension can be an important causal factor.

CASE REPORT

A 28-year-old woman had had a normal weight until 1 year after marriage when her husband was ordered overseas. She had been an orphan, was emotionally immature, and became depressed and extremely lonesome. When her husband returned 2 years later she had gained nearly 100 pounds. She decided her husband was ashamed of her because she was fat. She was unhappy, had frequent crying spells, consoled herself by eating, and continued to gain weight. She was treated by multiple glandular preparations including anterior pituitary extract and testosterone. When she did not improve she was hospitalized as a refractory endocrine problem. During the course of her study, the results of which were normal from a metabolic standpoint, a 600-calory diet was prescribed and she lost 40 pounds in 2 months. In the first week of treatment she had fainting spells that she attributed to lack of food. Her blood glucose was always normal at these times. Enough dextro-amphetamine sulfate was given to produce anorexia and the attacks ceased. She gradually came to recognize the fact that her polyphagia resulted from emotional stresses rather than from a physical need for food. Within 2 weeks she had become accustomed to the small meals, was encouraged by her weight loss, and the dextro-amphetamine sulfate was discontinued. She continued to lose weight after leaving the hospital.

TREATMENT

Many patients are unaware of the threat to life that obesity entails, and they can scarcely be expected to take their condition seriously until they acquire this information. It should be re-emphasized that cardiac and renal disease, glycosuria, and hyperglycemia are urgent indications, rather than contra-indications, for radical weight reduction. If patients with these diseases are obese, weight reduction is often the most effective therapy that can be given. Foremost in the treatment of obesity is caloric restriction. Best results are obtained by definite restrictions. Hunger pangs are no worse on a 400-calory diet than on a 1,400-calory diet and the weight loss is much more gratifying. There is generally no danger from such sharp caloric restriction. Obese patients who have subsisted on 450 calories daily were found to remain in nitrogen balance if they got 60 gm. of protein daily.

One of Newburgh's (*18*) patients was maintained for 1 year on a 300-calory diet. He lost 286 pounds and his health was definitely improved. The patient must be convinced that hunger is a normal healthy sensation and eating should stop short of satiation. He can be assured that if he will stick with the diet for 2 or 3 days the stomach will become accustomed to the lessened intake. The diet offered should be well balanced, high in protein, but extremely low in fat and carbohydrate. Protein has the advantage of its high satiation effect. Meat with all fat removed, fish, shrimps, oysters, skimmed milk, uncreamed cottage cheese, and unsweetened gelatin may be eaten freely. Sugar and butter are restricted and bread is allowed sparingly. Desserts and pastries have no place in the diet of obese persons. Cooked fruit and coffee should be sweetened with saccharin and vegetables flavored with only salt and condiments. A 400- to 600-calory diet is usually preferred. A daily multivitamin capsule is often of value as a means of reassuring the patient that he will not develop a deficiency disease. On such a diet the average patient can be promised a weight loss of 3 to 4 pounds a week. Both patient and physician should be acquainted with water swings in which periods of eliminating water often alternate with periods of retention. Some patients may fail to show weight loss for as long as 2 weeks but this will always give way to a subsequent rapid loss so that the end result will coincide with the estimated loss.

It must be remembered that each patient is an individual problem and the effort should be made to understand and correct the factors which produce obesity. Once the desired weight has been reached, attention should be given to the establishment of dietary habits that will maintain it. It often helps to tell women that continual fluctuation of their weight predisposes to the formation of wrinkles. The patient should visit the physician frequently in the early course of dieting. Otherwise there is a tendency to postpone the dieting until the time for the patient's return visit. Having lost no weight, he is ashamed to return and decides to try some magic cure a neighbor has recommended or go to another physician.

Another approach to female patients is to tell her that she is 130 pounds of her charming self and 100 pounds of inert fat. An obese patient may also be told that for him to be fat is equivalent to carrying a neon sign stating, "I am unhappy." Thyroid extract is indicated in myxedema only. The obese patient is already metabolizing more energy than the normal person just to maintain his corpulent state. To add thyroid extract is like giving it to the thyrotoxic patient who has a basal metabolic rate of plus 50. The increased mortality in these persons is caused by the strain placed on their vital organs by the increased metabolic demands. The object of therapy is to decrease that

load, not add to it. In general the same thing applies to vigorous exercise, it is not only dangerous and unwise for most obese persons, but it is relatively ineffective. A fat man must play 18 holes of golf to lose 4 ounces or walk 36 miles to lose a pound (*18*). It is easier not to eat so much in the first place. Massage may reduce the masseur but will have no such effect on the recipient.

Although the dangers of obesity are recognized and its correction involves nothing more than a decreased intake of food, many people lack the will power to push the dinner plate from them and they remain overweight. Amphetamine and a related series of drugs have proved valuable in promoting weight reduction (*26*). They do not increase the metabolic rate but produce their effect by inducing anorexia. If given in large enough doses to an experimental animal, the animal will actually starve in the presence of food. The drug is equally effective in animals in which the gastrointestinal tract has been denervated, which indicates the anorexia is central in origin. With recommended doses, undesirable side effects such as insomnia and nervousness are not serious and disappear on withdrawal of the drug. No physical addiction to these drugs has been demonstrated. Although some have contended that amphetamine is contra-indicated in the presence of hypertension, hypertensive patients are often the ones who need it most. Freed (*25*) gave amphetamine sulfate to 200 hypertensive patients in combination with phenobarbital three times daily and 196 of them showed a reduction in blood pressure.

Dextro-amphetamine sulfate is the drug of choice because of its effectiveness and the low incidence of undesirable side effects (*27*). Some patients, however, do better on one of the other preparations. The effective dosage is variable and may be from 5 to 50 mg. daily. The patient is usually started on 2.5 to 5 mg. 1 hour before each meal and the dose is gradually increased if this does not prove effective. Ideally, the patient should restrict his caloric intake without the use of these drugs. If he fails, drugs should be used as an adjunct since the beneficial effects from their use has greatly overbalanced any ill effects observed.

CONCLUSIONS

Physicians, regardless of their special fields of interest, see many obese patients. By educating each overweight patient to an appreciation of the dangers inherent in his condition and teaching him how to correct it, we can promise him a longer and healthier life. As physicians we should not neglect this opportunity to prevent or postpone the development of such causes of death as heart disease, cerebral hemorrhage, cancer, and diabetes.

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BLOOD VOLUME DETERMINATIONS IN THE UROLOGICAL PATIENT: An Adjunct in Preoperative and Postoperative Management, by Gladen E. Hamilton, *Lieutenant Colonel (MC) U. S. A.*, and Raymond J. Getz, *Major (MC) U. S. A.* Journal of Urology **62**: 607–616, Oct. 1949.

The blood volume was determined in 40 patients who were poor surgical risks. While these determinations have been employed for several decades by physiologists, only recently a method sufficiently accurate for general employment has been popularized. The Evans blue-dye technique, developed mainly by Gregersen, has made possible the performance of these determinations in any well-equipped hospital. The method consists of the electrocolorimetric measurement of the intensity of a dye 10 minutes after it is injected intravenously into the patient and comparison with a known standard. Weight loss in these patients was not constantly indicative of the blood-volume deficit. Deficits in 8 patients, who apparently had lost no weight, averaged 30 percent. There was no constant relationship between the blood volume and red blood cell counts, hematocrit, and hemoglobin determinations. The majority of the patients who had adequate replacement therapy recovered uneventfully following operation. In this series the correction of blood-volume deficit by whole blood transfusions was considered to be the most important single factor in the preparation of these patients for operation and their satisfactory postoperative course. The advantage of adequate replacement therapy after blood-volume determination will become more evident in the future by the reduced incidence of operative shock, postoperative wound dehiscence, infection, and poor wound healing.—*Abstract.*

Parathyroid Adenoma

Report of Two Cases

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PRIMARY hyperparathyroidism is caused by excessive formation of parathyroid hormone. This may in turn be caused by a single adenoma, multiple adenomas, a carcinoma, or idiopathic hyperplasia of the parathyroid glands. In many undiagnosed early cases of hyperparathyroidism, with a few significant symptoms, the diagnosis could have been made if estimates of blood calcium had been made as part of the clinical studies of patients having routine physical examinations (*1*). Norris (*2*) has recommended that case reports of all cases of primary hyperparathyroidism be published, with a view to clarifying the unsolved problems connected with this disease.

CASE REPORTS

Case 1.—A 45-year-old soldier entered this hospital on 11 March 1949 complaining of postprandial discomfort, nausea, and vomiting of about 9 years' duration. He was hospitalized at the time of the onset and roentgenographic studies revealed a chronic duodenal ulcer. He was discharged and instructed to take a bland diet for a short time. His symptoms for the next 7 years had been mild. In November 1947 his ulcer recurred. He was transferred to this hospital in January 1948 and was again given a bland diet; and his symptoms were relieved. In October 1948 he had a severe cold and voided some dull red urine. On 20 February 1949 he had anorexia, nausea, and vomiting. He improved on a milk diet and was well until 7 March. At that time he had an aching pain in both testes associated with mild tenderness in the right costovertebral angle. Sexual excitement aggravated the testicular pain. The pain in the right costovertebral angle persisted, and was associated with oliguria, but there were no other urinary symptoms. He continued to have nausea and vomiting after eating until the time of admission to this hospital.

Physical examination revealed a blood pressure of 170/100, mild tenderness in the right costovertebral angle, and bilaterally hyperactive reflexes. The leukocyte and differential counts, the hemoglobin, and the erythrocyte count were normal. A roentgenogram of the abdomen revealed an area of calcification overlying the sacrum and right pelvis, and a recheck revealed two small areas of calcification in the region of the lower pole of the left kidney. There was also

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an area of calcification, 1.3 by 0.3 cm., overlying the right side of the sacrum. A tentative diagnosis of chronic duodenal ulcer and renal calculi was made.

Phenobarbital, 0.1 gm. three times a day, tincture of belladonna, and a bland diet was prescribed. The symptoms of gastric retention were promptly controlled. On 22 March intravenous pyelograms revealed small calcifications in the lower poles of both kidneys. Function was good bilaterally with normal-appearing renal pelves. The calyces were incompletely outlined. In the region of the lower end of the right ureter there was an oval calcification, 12 by 6 mm., that gave the appearance of a ureteral calculus. The serum calcium was 11.7 mg. per 100 cc. on 15 March, and 14.1 mg. per 100 cc. on 23 March with a serum phosphorus of 2.8 mg. per 100 cc. A diagnosis of parathyroid adenoma was made. The urologist advised the removal of the calculus in the lower third of the right ureter before exploration for the parathyroid adenoma. On 25 March under spinal anesthesia a right ureterolithotomy was performed. The patient's postoperative course was uneventful. He was transferred to the general surgical service on 2 April. His serum calcium remained around 14.1 mg. and his serum phosphorus remained around 2.4 mg. per 100 cc. His 24-hour urine contained 0.4 gm. of calcium and 0.83 gm. of phosphorus. A roentgenographic survey of the skeleton revealed no abnormalities. His serum alkaline phosphatase was 9.3 units and his acid phosphatase was 0.18 units.[2]

On 21 April under sodium pentothal, nitrous oxide, and oxygen anesthesia the parathyroid glands were explored. On exploring the right lobe of the thyroid numerous small nodules were noted throughout the gland. The lower pole of the right lobe was explored first in accordance with the view that this is the most common site of a parathyroid adenoma (*2*) In this region a red-brown mass, about 3 by 1.5 cm., was identified and separated from the lower portion of the right lobe of the thyroid by blunt dissection. It was found to have its own vascular supply and to be entirely separate from the true capsule of the thyroid. The specimen was immediately sent to the laboratory for frozen section. Following this the upper portion of the right lobe, the left lobe, and the area between the esophagus and trachea was explored with no evidence of abnormal parathyroid glands. By this time a report had been received from the laboratory that the removed specimen was a parathyroid adenoma. Before closing the wound a specimen of blood was removed from the anterior jugular vein and sent to the laboratory for serum calcium and phosphorus determinations. This revealed the serum calcium to be 11.3 mg. per 100 cc. and the serum phosphorus to be 3.0 mg. per 100 cc. Postoperatively the patient had no signs of parathyroid tetany. His serum calcium gradually fell to 10.3 mg. per 100 cc. on the fifth postoperative day and the serum phosphorus remained unchanged. He regained his strength rapidly. A roentgenogram on 13 May revealed no change in the renal calculi. The patient was seen in the follow-up clinic on 14 August at which time he stated that he had not felt so well in years. His ulcer symptoms had not returned.

Pathologic findings

The specimen was a pear-shaped, relatively smooth, rubbery mass of tissue, which measured 0.4 by 1.5 by 3 cm. and weighed 3.1 gm. It was covered by a membranous capsule (fig. 1). The cut surface was homogeneous, compact, and pink-tan. Microscopically the specimen was extremely cellular and showed a thin, unbroken, connective tissue capsule. The cells were arranged in cords and

[2] Shinowara, Jones, and Reinhart method.

Figure 1.—Case 1. Parathyroid adenoma removed from patient.

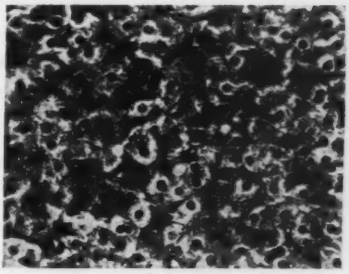

Figure 2.—Case 1. Microscopic appearance of parathyroid adenoma.

compact acini supported on a scant connective stroma, and separated occasionally by sinusoidal vascular channels. Generally, the cells presented a broad eosinophilic cytoplasm and a small dark round nucleus (fig. 2). The diagnosis was parathyroid adenoma.

Case 2.—A 57-year-old housewife entered this hospital on 11 August 1949 with a history of back pain and lower abdominal pain of 1 day's duration. Three years before she had had an attack of right renal colic but no nausea, vomiting, or hematuria. Roentgenograms at that time revealed no evidence of calculi, but there was some evidence of a kink in the ureter. Two years before admission she had had pain in the left flank without nausea, vomiting, or hematuria. On four occasions in the week before admission she passed slightly blood-tinged urine. On the night before admission she had urinary urgency and frequency and distress in the lower midportion of the abdomen but no nausea, vomiting, or hematuria. On the day of admission she complained of lower abdominal distress and lumbar pain bilaterally.

Physical examination revealed a blood pressure of 150/85. There was tenderness in the left flank and pain in the left costovertebral angle. A tentative diagnosis of renal calculus in the left kidney was made. The leukocyte and differential counts were normal. The hemoglobin was 12.8 gm. The urine was essentially negative. On 18 August the serum phosphorus was 2.3 mg. per 100 cc. and the serum calcium was 13.2 mg. per 100 cc. On 12 August a roentgenogram of the abdomen showed some calcific density in the region of the left kidney. Intravenous pyelograms on 15 August revealed a calcific density in the distal extremity of the left ureter. On 19 August with a ureteral catheter in place, roentgenograms revealed the previously described opacity lying immediately to the side of the catheter in the lower one-third of the ureter.

On 19 August through a cystoscope a calculus was removed from the left ureter with an Ellik loop. A recheck of the serum calcium and phosphorus showed them to be elevated; a diagnosis of parathyroid adenoma was made. On 29 August a classical collar incision was made in the neck and exploration for adenoma of the parathyroid was performed. Exploration of the right lobe was negative. Exploration of the left lobe revealed an elliptical mass, 2.5 by 2 cm., below the lower pole of the thyroid nested in the branches of the inferior thyroid artery. Two small vessels were seen entering the upper pole of the tumor. The red-brown tumor which was slightly darker than the thyroid tissue was removed. Postoperatively the serum calcium fell and the

serum phosphorus slowly returned to normal. The patient promptly regained her strength. At no time was there evidence of tetany. She was discharged on 8 September, at which time she was completely asymptomatic.

Pathologic findings

The specimen measured 1.7 by 1.2 by 1.1 cm. and weighed 1.8 gm. (fig. 3). Microscopic section showed partial encapsulation of cellular stroma within a loosely interwoven network of fibrous tissue elements. The cellular stroma was composed principally of closely packed cells which were segregated into acinarlike follicular arrangements by the interlacing fibrous tissue elements. The majority of the cells had dark-staining nuclei with relatively abundant cytoplasm. Occasional cells showed deep-staining acidophilic cytoplasm with multiple nuclei. The diagnosis was parathyroid adenoma.

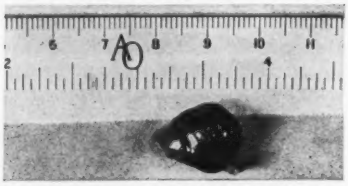

Figure 3.—Case 2. Parathyroid adenoma removed from patient

DISCUSSION

Black (*3*) reviewed a series of 63 cases at Mayo Clinic in 1946 and found that the condition was almost equally distributed between the sexes (31 women and 32 men) and the highest age incidence was in the fourth decade. The weight of the adenomas varied from 0.1 to 101 gm., almost 50 percent weighing 2.5 gm. or less. Norris (*2*) reviewing 322 cases of patients with parathyroid adenoma observed from 1903 to 1945 inclusive, noted the age incidence as being between 14 and 77 years with the maximum incidence between 40 and 50 years of age; in 317 cases there was a sex predominance of women over men in the approximate ratio of 3:1 in single adenomas and 4:1 in multiple adenomas. Of this group he found multiple adenomas in 20 instances or 6.2 percent while a single adenoma existed in 302 cases or 93.8 percent. The location of the tumor was recorded in 251 cases. In 132 cases (52.6 percent) the adenoma occurred on the right side and in 119 cases (47.4 percent) it was found on the left side of the neck. The weight of the adenoma varied from 0.4 to 120 gm. (average 12.7). The adenoma is usually well encapsulated and soft with a smooth surface. Through the capsule the adenomas often appear gray-brown. The cut surface is usually moist, homogeneous, and yellow-brown. Associated clinical findings include osteitis fibrosa and renal lithiasis alone or combined.

The signs and symptoms can best be divided into (*a*) those caused by hypercalcemia, consisting chiefly of muscle weakness and decreased muscle excitability such as constipation associated with nausea and vomiting, (*b*) those referrable to the urinary tract, and (*c*) those referrable to the skeletal system such as skeletal pain, epulides, and pathologic fracture (*4*).

Albright and Reifenstein (*5*) have divided the clinical types of primary hyperparathyroidism into (*a*) those with bone disease and without kidney disease, (*b*) those with bone disease and with kidney disease, (*c*) those without bone disease and with kidney disease, and (*d*) those without bone disease and without kidney disease. With only the findings of hypercalcemia, hypophosphatemia, hypercalcinuria, and hyperphosphaturia the diagnosis may be established with complete certainty (*3*). These characteristic findings might, however, be modified in cases of chronic renal disease with retention of metabolites, and retention of phosphorus might occur with consequent depression of the level of calcium in the blood. As the best method of establishing this Black (*3*) suggested that in surgical exploration for parathyroid adenomas a fairly complete dissection should be performed on the first side explored before crossing the midline. He is opposed to performing an exploration of the anterior superior mediastinum at the time when the cervical and posterior superior mediastinal exploration is performed, if the adenoma is not found in the neck. Instead he recommends performing the anterior superior mediastinal exploration after the cervical incision is well healed and after it can be demonstrated that the patient has not been cured.

The only form of acceptable therapy is complete surgical excision of the tumor. When the parathyroid glands are removed, there then results in this sequence: (*a*) an immediate decrease in phosphorus excretion in the urine, (*b*) an increase in serum phosphorus, (*c*) a fall in serum calcium, and (*d*) a decrease in calcium excretion in the urine. The patient's electrolyte patterns return to their normal state. If parathyroid extract were given to a normal person a reversal of these metabolic changes would have occurred but in the same sequence. The parathyroid hormone acts on the electrolyte equilibrium of the body fluids and the bone changes, when they occur, are secondary to the chemical changes (*5*). Finally Cope (*6*) states:

> The cornerstone to successful surgery of the parathyroids is a positive diagnosis. An exploratory operation to confirm or disprove a doubtful diagnosis has little or no place in the field. The findings of the laboratory are more exact than the dissection of the surgeon, and there is no point in the operation, at which the operator may lay down his scalpel and find comfort in having disproved the diagnosis.

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MINIMUM POSTOPERATIVE MAINTENANCE REQUIREMENTS FOR PARENTERAL WATER, SODIUM, POTASSIUM, CHLORIDE, AND GLUCOSE, by Robert Elman, M. D.; Richard A. Lemmer, M. D.; Theodore E. Weichselbaum, Ph. D.; James G. Owen, M. D.; and Richard W. Yore, M. D. Annals of Surgery **130:** 703–722, Oct. 1949.

Balance studies were carried out in 40 surgical patients on a completely intravenous intake for 96 postoperative hours, and in a few cases during several preoperative days. Study of the urinary output included volume, specific gravity, creatinine, sodium, potassium, chloride, phosphate, nitrogen, glucose, and acetone. Blood levels of sodium and potassium, chloride, CO_2, plasma, protein, and red cell volume were also measured before and after each study.

With an intake limited to 2 liters a day there was an adequate urinary output during the 4 postoperative days of about 1 liter except for a moderate oliguria during the first postoperative day. The oliguria was accompanied by a decreased creatinine excretion with no change in specific gravity.

With no electrolyte intake, the body rapidly conserves sodium and chloride, but not potassium and phosphate. The cumulative loss during 4 postoperative days averaged about 4 gm. calculated as sodium chloride and 6 gm. calculated as potassium chloride. No changes in plasma levels of sodium, potassium, CO_2, proteins, or in red cell volume were observed on this intake.

With an intake of 9 gm. of sodium chloride a day, there was a definite lag in excretion so that of the 36 gm. injected, an average of about 14 gm. was retained. The loss of potassium, however, was the same.

It is estimated from these findings that an intake of 2 liters of water plus 2 to 4 gm. of a mixture of sodium and potassium chloride (or gluconate) would meet the minimum requirements for these elements in the postoperative patient.

Calculation of the potassium-nitrogen excretion ratio suggests that only part of the potassium loss originated from the break-down of tissue protoplasm.

The nitrogen sparing effect of 200 gm. of *d*-glucose was not significantly greater than 100 gm. of *d*-glucose. On the other hand, because of an undoubted disturbance in carbohydrate metabolism, acetonuria was more frequent under the latter than under the former intake. Glycosuria conversely was greater with a 200 gm. intake as compared with a 100 gm. intake. In order to determine the minimum requirements for *d*-glucose, further observations will be necessary, particularly with regard to the influence of the rate of injection.—*Abstract.*

Acute Disseminated Lupus Erythematosus

Report of Three Cases in Young Polish Men

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FROM July 1947 to January 1948, three cases of acute disseminated lupus erythematosus were seen at the United States Naval Hospital, Philadelphia, Pa. These young men were of pure Polish extraction and all had type A blood.

A review of the literature showed no definite information concerning racial predilection for this disease. In 1942, Gahan (*1*), reviewing the literature for the geographic distribution of lupus erythematosus, found the incidence of the patients with new cutaneous diseases in the United States to be 0.4 percent and no appreciable difference in any part of the world except in the tropical countries where it is rare among the colored races.

CASE REPORTS

Case 1.—T. L. S (*2*), a 35-year-old white man of pure Polish descent, had sore throats frequently as a youngster and as an adult. Five months before admission, he had sinusitis and was treated with penicillin irrigations. At this time he noticed a small erythematous macule over the left malar eminence. Three months later, he had a septic-type fever, chills, generalized malaise, abdominal pain, nausea, vomiting, and diarrhea of 8 days' duration. He believed that there was an accentuation and spread of the erythematous patch over the left cheek, bridge of the nose, scalp, and ears during this time.

Physical examination on admission showed a well-developed and well-nourished but very sick white man with the following outstanding physical findings: inflammation of the pharynx; a snus tachycardia; and generalized abdominal tenderness.

The laboratory findings were: Hemoglobin varied from 11.5 to 12.5 gm.; red blood cell count varied from 3.9 to 4.5 million; and white blood cell count varied from 5,050 to 11,200 with a slight shift to the left; type A blood; blood Kahn test and all blood cultures were negative; urine concentrated to 1.015, with a slight

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trace of albumin, an occasional red blood cell, and 2 to 3 white blood cells in the sediment; blood urea nitrogen, 16.5 mg. per 100 cc. blood; chest roentgenogram was negative; sputa, negative for tubercle bacilli; electrocardiogram showed ST segment and T-wave changes in all leads as well as right axis deviation and the graph was consistent with acute pericarditis.

Treatment consisted of sulfadiazine, 10 gm. daily in divided doses, parenteral fluids, transfusions, large doses of ascorbic acid, 50 mg. of pyribenzamine every 4 to 6 hours by mouth, digitalis, oxygen, and sedation.

His temperature hovered about 105° F.; pulse, 140; respirations, 40; and blood pressure, 120/85. Three days after admission the skin lesions were less erythematous but new lesions appeared on the buttocks. He became progressively more stuporous and dyspneic. With the onset of clinical evidence of cardiac failure, digitalis was administered. Respirations became more labored and he died 8 days after admission. Terminally, all his lesions became purpuric.

Necropsy report.—Atypical verrucous endocarditis, myocardial fibrosis, bronchopneumonia, connective tissue degeneration around blood vessels, and wire looping of the glomerular capillaries.

Case 2.—A. J. L., a 25-year-old white man of pure Polish descent, had had frequent attacks of urticaria precipitated by the ingestion of citrus fruits and tomatoes. At the age of 18, he had a reaction to tetanus antitoxin, manifested by partial collapse and urticaria. For the last 2 years his wife had noticed that he had a malar flush whenever he drank alcoholic beverages or became excited.

He was first admitted to the hospital in August 1947 because of fever and multiple joint pains. Physical examination showed an inflamed throat and several swollen phalangeal joints. Eight days after admission an abscessed tooth was removed; no change occurred in his clinical picture. Electrocardiogram was negative; blood sedimentation rates were elevated; hemoglobin, white blood cell count, differential count and urinalysis were negative; roentgenograms of the small bones of the hands showed changes consistent with early rheumatoid arthritis. He was hospitalized for 27 days at this time and was discharged with instructions to receive from his physician a course of treatment with proprietary streptococcal vaccine for his arthritis.

During his 24 days at home he continued to have generalized arthralgia and fever. Two weeks before the second admission he noted an erythematous eruption on the malar areas. A week before the second admission he was told he had a similar eruption at the base of his spine. During this week while he was treated with the vaccine, he had a sore throat, chills, anorexia, nausea, and diarrhea.

The second-admission physical examination showed a very sick patient with a follicular pharyngitis; grade 2 aortic systolic murmur; sinus tachycardia; blood pressure of 112/64; and a few moist inspiratory râles at the bases. The remainder of the examination was not remarkable.

The laboratory findings were: hemoglobin, from 11 to 12 gm.; red blood cell count varied from 3.2 to 4.3 million; white blood cell count varied from 4,500 to 7,800 with a shift to the left; normal platelet count, coagulation, and bleeding time; type A blood; Kahn test and blood cultures were negative. Hemolytic streptococcus was cultured from the pharyngeal ulcer. Urine showed a slight trace of albumin, 2 to 6 red blood cells, and 2 to 10 white blood cells; it concentrated from 1.010 to 1.018; blood urea nitrogen, 14 mg. per 100 cc.; admission roentgenogram was negative, but final examination showed bilateral pleural effu-

sion; electrocardiogram showed low voltage and diphasic QRS waves in lead 1 and 3; a biopsy of skin from the face showed changes consistent with acute disseminated lupus erythematosus.

He was treated with 100,000 units of penicillin intramuscularly every 3 hours, large doses of vitamin C parenterally, 50 mg. pyribenzamine by mouth every 6 hours, frequent blood transfusions, parenteral fluids, digitalis, oxygen, sedation, and cautery of the pharyngeal ulcer.

During this course temperature varied from 99° to 105° F.; pulse from 80 to 130; and respirations from 20 to 40 per minute. After 3 days of hospitalization he appeared to improve, but the right tonsillar ulcer was not improved. Six days after admission, there was an extension of the skin eruption to the lower anterior chest, thighs, and feet, while the face lesions were less erythematous. Eight days after admission he had a gallop rhythm and evidence of bilateral pulmonary edema. Digitalis was administered but the patient continued to be dyspneic and to fail. He died 17 days after admission.

At necropsy, there was hypertrophy, dilation, and fibrosis of the heart, atelectasis of both lungs, bilateral pleural effusion, hyalinization and thickening of the arterioles of the spleen, cirrhosis of the liver, and thickening of the capillary loops of the kidney.

Case 3.—F. C. Z., a 20-year-old white man of pure Polish extraction, had eczema as a child, and had diarrhea whenever he drank milk or ate tomatoes. He had recurrent hay fever since the age of 12. One year before his first admission he had an attack of hives, cause unknown.

He was hospitalized with pleurisy for 3 weeks in December 1946. During this time he was treated with one of the sulfonamides. Because of a persistent, generalized, nontender lymphadenopathy, he was sent to a naval hospital for medical observation. Heterophil agglutinations, chest roentgenograms, white blood cell counts, urinalyses, and an electrocardiogram were negative. Two lymph node biopsies showed only hyperplasia. During his stay, he had recurrent episodes of low grade fever and migratory painful joint swellings. All the blood cultures were negative. He was again treated with one of the sulfonamides as well as penicillin, with no change in the clinical picture. After 3 months of hospitalization he became afebrile, relatively asymptomatic, and was given a trial of duty. Following his discharge from the hospital, he had fatigue, anorexia, arthralgia, and a 20-pound weight loss. However, he noted some decrease in the size of lymph nodes.

Four months later he was readmitted because of tender swelling of his right knee for 1 month's duration. He had felt feverish during this attack. He denied any preceding sore throat, conjunctivitis, or urethral discharge. Physical examination showed sinus tachycardia; slight cardiac enlargement with a grade 2 mitral systolic murmur; blood pressure was 140/80; a tender swollen right knee; and generalized nontender lymphadenopathy. The clinical diagnoses considered were acute rheumatic fever or periarteritis nodosa. Electrocardiograms and antistreptolysin titer were not informative. Lymph node biopsy again showed hyperplasia. Twenty-eight days after his admission an erythematous eruption appeared on the malar areas, across the bridge of his nose, on his ears, and in his scalp. A specimen of the involved skin was taken for biopsy and changes consistent with acute disseminated lupus erythematosus were reported. He had hemorrhage into the left fundus and ptosis of the left eyelid. He continued to have a low grade fever. The facial eruption became less erythematous but more pigmented. He was sent home for convalescence but was readmitted in 6 weeks. Upon his return, he was given several blood transfusions.

On this final admission he appeared very sick and debilitated: He had lost 40 pounds within the last 6 months. His respirations were rapid and labored, and blood pressure was 140/110. He had a patch of consolidation in the base of the lower lobe, left lung, which persisted throughout his clinical course.

Laboratory findings.—Hemoglobin varied from 8 to 14 gm.; red blood cells varied from 2.2 to 3.7 million; white blood cells varied from 4,000 to 20,000 with a definite shift to the left; type A blood; blood Kahn tests, blood cultures, and agglutination test were all negative; 333 units antistreptolysin titer; and urine showed 2 plus albumin, occasional 1 to 2 red blood cells, 6 to 8 white blood cells, and an occasional granular cast. Nonprotein nitrogen was 40 mg. per 100 cc. blood. Two electrocardiograms appeared to be consistent with pericarditis. Roentgenograms showed a mottled density at the left base and were interpreted as atypical pneumonia. The last roentgenogram taken 1 day before his death showed evidence of multiple infarctions with bilateral congestion. Throat cultures were negative for hemolytic streptococcus; sputa repeatedly negative for tubercle bacilli.

Treatment consisted of 50,000 to 100,000 units of penicillin intramuscularly every 3 hours, 14 gm. of streptomycin intramuscularly, large doses of vitamins parenterally (particularly vitamin C), 5 cc. of crude liver extract intramuscularly daily, 50 mg. of benadryl by mouth every 6 hours, frequent blood transfusions, parenteral fluids, plasma, digitalis, ferrous sulfate, oxygen, and sedation.

Repeat biopsy from skin of the face before death showed atrophic epidermis, mononuclear cell infiltration, and basophilic degeneration in the corium. This picture was again consistent with acute disseminated lupus erythematosus.

Ten days after admission, nontender erythematous macules appeared on his hands which faded in 3 days. His course continued downhill. Thirty-two days after admission, one-half gm. of streptomycin every 6 hours was prescribed. Four days later, he had a pulmonary infarct, but presented no evidence of thrombophlebitis of his legs. Oxygen and sedation were administered. A gallop rhythm and evidence of pulmonary edema appeared and digitalization was employed. For the next 5 days he complained of recurrent episodes of chest pain. He became progressively more dyspneic and died on his forty-first hospital day.

Authorization for necropsy was refused.

SUMMARY

Three cases of fatal acute disseminated lupus erythematosus occurring in young Polish men are reported. These cases showed certain similarities: pericardial involvement as indicated by electrocardiogram; type A blood; blood Kahn test and blood cultures were negative; elevated blood sedimentation rates; and urinary changes. There was definite history of allergy in two cases. The diagnoses were confirmed by skin biopsies in which no blood vessel changes were seen. Autopsy in two cases showed connective tissue degeneration about the splenic blood vessels and in the myocardium and wire-looping of glomerular tufts.

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Subacute Granulocytic Leukemia

Report of a Case Following Infectious Mononucleosis

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EXTENSIVE review of the literature fails to reveal any report of the association of infectious mononucleosis with malignancy of the reticulo-endothelial system. Reports have been made of the resemblance of certain cases of lymphocytosis, including infectious mononucleosis, to acute leukemia; the clinical course in these instances was benign (*1*) (*2*) (*3*). However, the unusual sequence of events in this case warrants this report.

CASE REPORT

T. C. S., a 20-year-old white man, was admitted on 22 April 1948, because of malunion of Pott's fracture, right ankle, which he sustained 1 January 1948.

He had no complaints except those relative to the right ankle which on examination revealed slight swelling and limitation of motion.

The remainder of the examination was normal. Routine blood studies showed: white blood cells 22,450; and hemoglobin, 12 gm. Repeated white blood cell counts showed a moderate leukocytosis and the differential studies showed abnormal lymphocytes typical of infectious mononucleosis. Heterophile agglutination tests on 10 May 1948 and 20 May 1948 were positive in dilutions of 1 : 448. A diagnosis of infectious mononucleosis was made and the patient was kept under observation.

During the 6-week period between the patient's admission to the hospital and 2 June 1948, he remained afebrile and symptom-free except for tenderness of the right ankle. The white blood cell count ranged from 22,000 to 46,000 and the differential studies remained unchanged.

Nine days later, the white blood cell count was 134,800; the red blood cell count was 2,630,000; platelet count, 95,200; and prothrombin content, 30 percent of normal. Microscopic examination of sternal marrow and peripheral blood smears revealed subacute granulocytic leukemia. At this time the heterophile agglutination test was 1 : 28.

The patient's subsequent course was rapidly downhill; and was characterized by profound weakness, fever, hepatomegaly, splenomegaly, and spontaneous hemorrhages. Treatment with repeated transfusions and urethane orally was of

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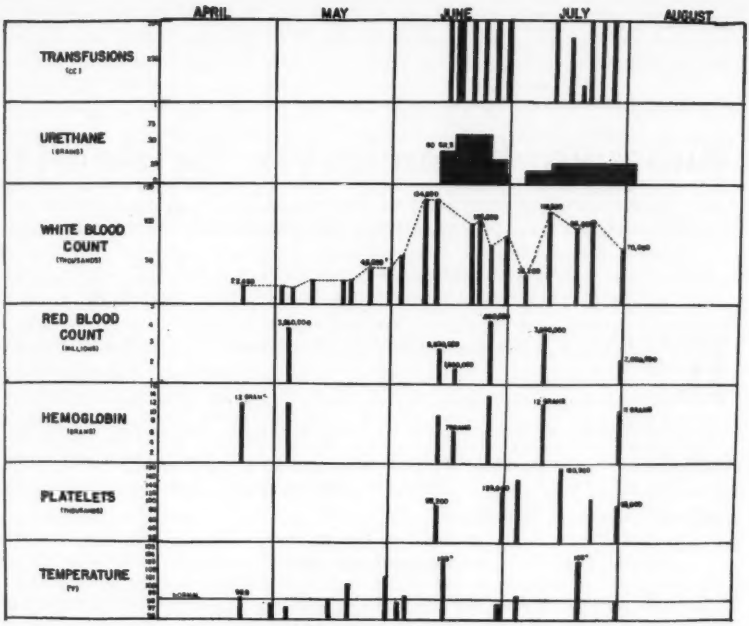

Figure 1.—Hospital course.

no avail, and the patient died on 9 August 1948. Autopsy performed at the Veterans' Hospital, Hines, Ill., revealed widespread leukemic infiltration and terminal multiple spontaneous hemorrhages. Figure 1 graphically illustrates the hospital course.

COMMENT

The sequence of events led to speculation but no conclusion. This patient was one of three typical cases of infectious mononucleosis in this hospital at the time. The clinical course of the other two was uneventful. Of further interest is the work of Weinstein and Fitz-Hugh (*4*) indicating that an increase in the heterophile agglutination titer does not occur in leukemia.

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Preservation of Neurotropic Viruses

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THE advantages of 0.2 percent bovine serum albumin in buffered saline solution over animal serum, as a diluent for influenza and yellow fever viruses in infectivity titrations, were described by Dick and Taylor (*1*). The chief advantages are (*a*) ease of preparation of the albumin solution; (*b*) its lack of specific or nonspecific virus inactivating substances (*2*) (*3*), (*c*) its ready sterilization; and (*d*) the clearness of the solution. This laboratory later found that serum albumin solution was a satisfactory diluent for a large number of neurotropic viruses in experiments on hemagglutination because it offered a nonagglutinating medium and no loss of titer of the virus was noted in the time taken to perform the test (*4*). The viruses employed were: Columbia SK, Columbia MM, and Mengo encephalomyelitis; encephalomyocarditis; Eastern, Western, and Venezuelan equine encephalitis; Japanese, St. Louis, and Russian Far East encephalitis; vesicular stomatitis (New Jersey and Indiana strains); West Nile disease; rabies; lymphocytic choriomeningitis; louping ill; herpes simplex; Theiler's disease (F. A., T. O., and GD–VII strains); and poliomyelitis (Lansing and MEF1 strains). In a single preliminary test with Eastern equine encephalitis virus, it was found that virus recovered from the brain and diluted in 10 percent normal rabbit serum had an LD_{50} titer of $10^{-8.5}$ while the same virus diluted in 0.2 percent albumin solution yielded an LD_{50} titer of $10^{-9.2}$.

It was desired to find out whether the albumin solution could replace animal serum for the preservation of neurotropic viruses for long periods of time and whether viruses in such solutions could be maintained in a mechanical refrigerator at $-20°$ to $-25°$ C. at sufficiently high titers (*5*). It has already been shown that electrically operated, mechanical refrigerators held at $-20°$ to $-25°$ C. have certain advantages over dry ice for prolonged preservation of certain viruses in serum suspensions. The object of this article is to describe tests on the maintenance of neurotropic viruses in the albumin solution stored

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in a frozen state in a mechanical refrigerator for varying periods of time up to 1 year.

METHOD

Crystallized bovine plasma albumin was prepared by following the directions given by Dick and Taylor (*1*). For storing viruses in the frozen state a 2 percent albumin solution was used; and for their dilution, as in infectivity titrations, 0.2 percent was used. The refrigerator was of the type used by Olitsky et al. (*5*). It was accidentally disconnected 5 months after the beginning of the test and on another occasion, 2 months later, failed to operate properly. As a consequence, the specimens were thawed twice for periods of time varying from a few hours to less than 36 hours. The viruses studied were those of Western equine encephalitis (Rockefeller Institute strain), St. Louis encephalitis (B–33 strain), lymphocytic choriomeningitis, and poliomyelitis (MEF1 strain). The neurotropic viruses were preserved in fresh, infected mouse brains made up as a 1 : 5 dilution in 2 percent albumin solution. Part of this was used for an initial infectivity titration. A number of the remaining specimens were placed in screw-capped nitrocellulose tubes and stored in the refrigerator which was held at −20° to −25° C. At 3-, 6-, 9-, and 12-month intervals each frozen suspension was thawed rapidly and an infectivity titration by the intracerebral route, in serial decimal dilutions, was made. The Swiss-W strain of mice was used for the titrations of the St. Louis encephalitis virus and the Rockefeller Institute strain was used for the others.

RESULTS

The results of the tests (table 1) revealed that stability varies with the virus employed. After storage the MEF1 virus retained its initial LD_{50} titer at least for the entire year. The other viruses studied were not so stable. The infectivity of Western equine encephalitis virus held up well for 9 months but after 12 months exhibited a drop of almost 3 logarithmic units from its initial titer. St. Louis encephalitis virus retained its LD_{50} titer during 3-month storage but

TABLE 1.—*Effect of storage of 1 : 5 virus suspensions in 2 percent albumin solution on infectivity titer*

Virus and original LD_{50} titer	LD_{50} titer after storage			
	3 months	6 months	9 months	12 months
Lymphocytic choriomeningitis $10^{-4.2}$	$10^{-4.6}$	$10^{-3.2}$	$< 10^{-0.6}$	----------
Lymphocytic choriomeningitis $10^{-5.6}$	$10^{-3.5}$	$10^{-3.4}$	$10^{-2.6}$	----------
Western equine encephalitis $10^{-7.5}$	$10^{-6.2}$	$10^{-6.2}$	$10^{-7.3}$	$10^{-4.5}$
St. Louis encephalitis $10^{-7.2}$	$10^{-7.2}$	$10^{-5.4}$	$10^{-4.6}$	$10^{-5.6}$
Poliomyelitis (MEF1) $10^{-3.6}$	$10^{-3.5}$	$10^{-3.5}$	$10^{-3.4}$	$10^{-4.3}$

was reduced about 2 logarithmic units after 6 months and was still infective after 1 year. The infectivity of the virus of lymphocytic choriomeningitis, however, fell off at 3 months and was greatly reduced after 6 months.

SUMMARY

The level of infectivity titer exhibited during prolonged storage in a frozen state at −20° to −25° C., and suspended in 2-percent bovine plasma albumin in buffered saline solution, varies with different viruses. The poliomyelitis MEF1 virus retained its original titer throughout a year while lymphocytic choriomeningitis virus showed a decrease at 3 months, the St. Louis encephalitis virus at 6 months, and the Western equine encephalitis virus at 12 months. The effect of two accidental thawings on the titer is unknown and it is not known what the results might have been if dry ice had been used instead of a mechanical refrigerator. All the viruses could be recovered by animal passage after storage for 6 to 12 months. Olitsky et al., using an adequate amount of normal rabbit serum instead of albumin solution for the preservation of certain neurotropic viruses in a mechanical refrigerator, recorded a definite reduction in titer of some of them at 3 and 9 months (*5*). The method here described for preserving viruses is applicable to conditions in which a buffered saline solution of bovine plasma albumin is desired as a substitute for animal serum, preserved in a refrigerator. The variations in the preservation of the viruses here studied would indicate that a pattern of infectivity after storage must first be determined for each virus before the method is generally adopted.

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Auricular Fibrillation Following Hypothermia

Report of a Case

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CLYDE J. DAWE, *Lieutenant, junior grade (MC), U. S. N. R.*[1,2]

COLD has both a direct and indirect effect upon the heart. In man, when the body temperature progressively falls to extremely low levels, the heart is first stimulated then depressed. This depression is characterized by a fall in heart rate, the appearance of arrhythmias, muffling of the heart sounds, and, eventually, heart failure. Electrocardiograms may show auriculoventricular block, intraventricular conduction defects, alteration of the S–T segments and inversion of the T waves. Auricular fibrillation is one of the arrhythmias which may supervene and the lower the body temperature the greater the likelihood of occurrence (*1*) (*2*). Tomaszewski (*3*), in reporting some observations in the case of a man who died following exposure to cold, illustrates the report with an electrocardiogram in which auricular fibrillation is probably present although this possibility is not mentioned by the author. Wayburn (*4*) describes the clinical findings in six cases of immersion hypothermia, two of which showed auricular fibrillation. Electrocardiograms were obtained in both instances, one of which was published. Inasmuch as there are few recorded instances of auricular fibrillation brought on by cold, the following case is reported.

CASE REPORT

C. G., a 32-year-old white man, was brought to the dispensary at Cherry Point, N. C., at 0200 on 16 November 1947. The previous afternoon he had gone fishing and, at approximately 2000, his boat overturned. He sat astride the boat submerged in cold water up to his nipples until rescued 6 hours later. The temperature of the water was not measured but the aerology department estimated it was between 55° and 58° F. During a 3-hour period just prior to immersion, he had drunk half a pint of whisky. The past history was noncontributory.

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[2] Inactive.

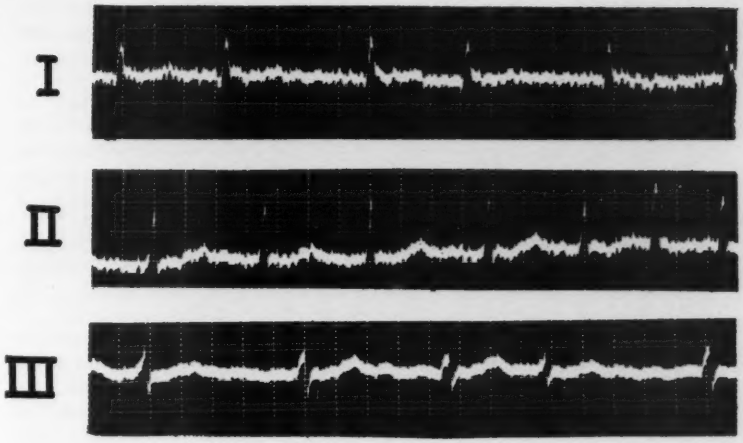

Figure 1.

On admission the patient was conscious but responded very sluggishly both to questioning and to physical stimulation. Examination revealed a well-developed muscular man appearing to be older than his stated age. The body temperature was not accurately determined inasmuch as the thermometer used could not record temperatures below 92.0° F., which was the oral temperature registered. He was moderately cyanotic and the skin was cold and

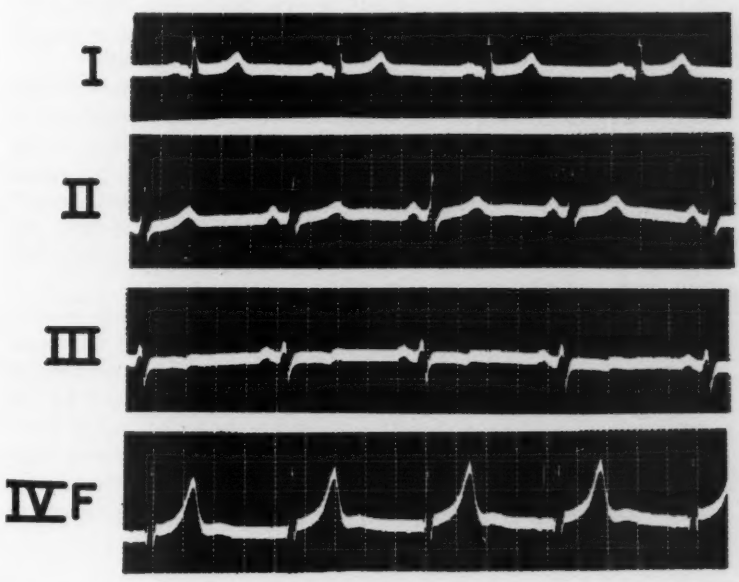

Figure 2.

wrinkled. He shivered intensely and kept curled up as tightly as possible. Examination of the lungs revealed no abnormality although auscultation was difficult because of the muscular tremor. There was difficulty in determining the size of the heart and a cardiac impulse could not be felt. The sounds were indistinct and the rhythm absolutely irregular with an average rate of 68. No murmurs were heard. The blood pressure was 100 mm. Hg systolic and 60 diastolic. An electrocardiogram (fig. 1) showed auricular fibrillation with the ventricular rate averaging about 75 a minute. The baseline was irregular, due to body tremor. The S–T junction was slightly elevated in lead 1 and the T waves were nearly isoelectric in this lead but upright in leads 2 and 3.

The patient, after being given an ounce of alcohol, hot coffee, and ephedrine (72 mg. intramuscularly), was gradually warmed under blankets. He responded quickly to therapy and 8 hours after admission he was ambulant. He rested the following day, then returned to work.

Eighteen days later he was asked to return for reexamination. He appeared to be 10 years younger than he did on the first admission and stated that he felt well. The heart was not enlarged and the apical thrust was easily palpable. The sounds were distinct, of good quality, and no murmurs were heard. The rhythm was normal at a rate of about 72. The blood pressure was 110 mm. Hg systolic and 64 diastolic. The remainder of the examination revealed no abnormalities. An electrocardiogram taken at this time (fig. 2) showed normal rhythm at a rate averaging about 65. The T waves were now tall and upright in lead 1.

DISCUSSION

The general features of this case illustrate the fact that persons who are not far from death as the result of hypothermia may be quickly restored to their previous state of health. In this regard, cold is almost unique among injurious agents and the explanation is largely to be found in the lowered metabolic activity of the body cells.

The effects of cold on the heart which were observed in our case were diminution in intensity of the heart sounds, feeble heart action, auricular fibrillation with slow ventricular rate, and lowering of the T-wave changes in the electrocardiogram may occur as the result of cooling the heart locally (*5*) (*6*) or of generalized hypothermia (*7*). Clinical studies suggest (*8*) and pathological studies show (*7*) that these T-wave changes may occur in the absence of structural damage to the myocardium.

With regard to the auricular fibrillation, two features are worthy of special notice, namely, the slow ventricular rate and the spontaneous return to normal rhythm. The former implies a considerable degree of auriculoventricular block which is probably caused by the direct effect of cold on the heart. The possibility of vagus overactivity must be considered but Tomaszewski (*9*) has shown that in animals, at least, slowing of the heart as the result of hypothermia may be independent of vagal activity. The spontaneous return to normal rhythm is characteristic in these cases.

The appearance of auricular fibrillation under conditions of hypothermia has not been satisfactorily explained. Vagus overactivity and alteration in the chemical and endocrine constituents of the blood have been mentioned as possibilities. However, there is no proof that any of these are important etiologic factors. One possibility that has not received attention is that, in contrast to many other organs, the heart must do considerable work regardless of how low the body temperature falls if the person is to survive. However, a point must be reached when the metabolism of heart-muscle cells is sufficiently reduced or otherwise interfered with so that contractility is faulty. This amounts to a local cause for failure and offers a reasonable explanation for the appearance of fibrillation in the auricles.

SUMMARY

A previously healthy young man nearly perished from hypothermia as the result of accidental immersion in cold water. Auricular fibrillation was among the clinical findings.

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Orthodiascopic Measurements During Fluoroscopy

A Device

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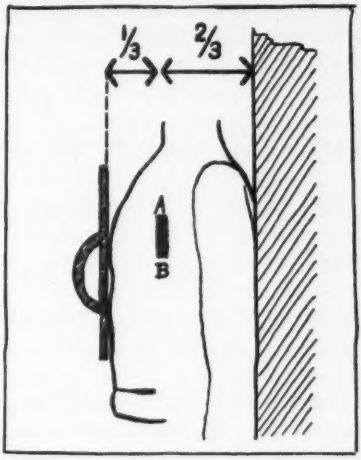
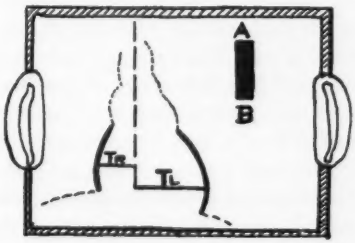
A VARIETY of procedures have been devised for the roentgenographic estimation of heart size but most of these have certain drawbacks which are well considered in various texts on cardiology such as the third edition of White's "Heart Disease." Even in teleoroentgenograms there is a distortion from divergent rays amounting to 5 to 8 percent depending on the tube-film and object-film distance. As a consequence the tables and nomograms for the prediction of normal teleoroentgenographic values differ from those for orthodiascopic reference. Furthermore the wide range of the normal heart size and shape in correlation with height, weight, and body surface area, makes the rigid application of so-called normal standards to borderline cases extremely hazardous. However, there is some merit in any simple procedure which introduces a quantitative element into clinical evaluations provided it is not slavishly followed.

The device described permits correction for the distortion of the ordinary vertical fluoroscopic image so that the actual transverse diameter of the heart may be recorded for comparison with tables of orthodiascopic normals or with subsequent observations on the same patient. It is a modification of Gubner and Ungerleider's method (*1*) for measuring heart size in miniature films and any credit for originality is entirely theirs. This modification eliminates the markings on the lead scale which are hard to read on the fluoroscopic screen and does away with the bracket for the support of the lead scale. It also avoids disturbing the screen-tube relationship when the patient, in the original method, steps aside to permit projection of the scale on the screen. Both methods are based on the assumption that a radiopaque body in the same plane as the heart will be enlarged on the fluoroscopic screen to the same extent as the heart shadow. The heart plane is usually one-third of the distance from the front to the





$$\frac{T_R + T_L}{X} = \frac{AB}{50mm}$$

Figure 1.

back of the thorax. This plane, usually in the anterior axillary line, is determined by actual measurement and a 50 mm. lead ribbon fixed to the chest at this point with a strip of cellulose tape. The accuracy of placement is easily verified by inspection in the lateral view during fluoroscopy. The limits of the lead ribbon's shadow in the A–P view are then marked with grease pencil on the fluoroscopic screen as a reference standard. At the end of a shallow inspiration the lateral borders of the heart are similarly recorded as indicated by the heavy lines in the diagram (fig. 1). It is evident, then, that the transverse diameter so obtained bears the same ratio to the actual transverse diameter as the magnified image of the lead ribbon bears to its actual length. A small slide rule will solve this simple proportion without recourse to pencil and paper.

If desired, the rest of the heart shadow (dotted lines) may be outlined with grease pencil and this diagram, along with the image of the lead standard of reference, transferred to tracing paper for future comparison. It is important that the ribbon be attached to the chest in a vertical plane as obliquity will introduce serious distortion.

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Continuous Spinal Anesthesia: The Ureteral Catheter (Tuohy) Technique

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IN 1939, Lemmon (*1*) described the first method for administering continuous (fractional) spinal anesthesia. He used an indwelling malleable needle in the subarachnoid space. In 1944 Tuohy (*2*) (*3*) (*4*) reported a second method in which a ureteral catheter was threaded into the subarachnoid space through a large gage spinal needle, this needle being immediately withdrawn. The primary objective of the Tuohy method was to overcome technical difficulties of the former technique such as: (*a*) relative ease of dislodgement of the malleable needle; (*b*) trauma to the tissues incident to leaving the needle in place; (*c*) remote hazard of breaking the needle in the tissues; and (*d*) need for a special mattress. Since the malleable needle technique has been evaluated by many investigators (*5*) (*6*) (*7*) (*8*) (*9*) (*10*) (*11*) (*12*) (*13*) (*14*), it was decided to study the catheter technique used at the United States Naval Hospital, Philadelphia, Pa., during 1947 and 1948. This article is a review of over 250 cases in which the ureteral catheter method was used for surgical anesthesia and also for several diagnostic and therapeutic procedures.

TECHNIQUE

Method.—The patient is placed in the lateral recumbent position for the lumbar puncture. The skin is cleaned with ether and tincture of merthiolate. After draping, a 1 percent procaine skin wheal is made over the lumbar interspace to be entered (usually the third, occasionally the fourth, and, rarely, the second.) Following infiltration of the interspinous ligament with 1 percent procaine, a 16-gage, 3½-inch Huber-point needle is introduced into the subarachnoid space. The needle is directed cephalad so that it makes an angle of approximately

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45° with the patient's back. As soon as clear flow of spinal fluid is obtained a graduated 3.5 Fr. ureteral catheter containing a wire stylet is threaded through the needle until it reaches the Huber point (care being taken not to lose an excessive amount of spinal fluid during this maneuver). The wire stylet is then slowly withdrawn as the catheter is simultaneously advanced beyond the point of the needle into the subarachnoid space for a distance of 4 to 5 cm. The stylet is then entirely removed, and the spinal needle withdrawn, leaving the catheter in place. If the catheter is properly introduced into the subarachnoid space, spinal fluid will drip freely from it. If, however, spinal fluid cannot be aspirated easily, the catheter is removed and reinserted because it is believed that the few failures early in the series were due to placing the catheter in the epidural space. When a paresthesia is noted on inserting the catheter and when it cannot be overcome by slight turn of the needle, the catheter and needle are withdrawn and reintroduced. On occasion the catheter cannot be passed beyond the end of the needle, apparently because of obstruction by the vertebral body when the needle is too far into the canal. This difficulty is encountered more frequently when the needle is perpendicular to the back rather than when in a somewhat cephalad direction. The catheter, once it has ben threaded beyond the point of the needle, must not be withdrawn, otherwise the Huber point may be sheared off within the subarachnoid space. When the catheter is satisfactorily in place it is connected to a 10 cc. Luer-Lok syringe and stopcock by means of a Borst adapter, and then fixed to the patient's back with adhesive tape. A small gauze pad is placed at the point where the catheter enters the skin to prevent kinking. The patient is then put into the desired position for injection of the anesthetic solution.

DRUGS

(*a*) *Preoperative medication.*—Most patients in the series receive pentobarbital sodium (0.1 gm.) the night before and the morning of the operation. Morphine sulfate and scopolamine (or atropine sulfate) in a 25 : 1 ratio are given routinely 1 hour before operation.

(*b*) *Pressor agents.*—Ephedrine sulfate (25 to 50 mg.) is given intramuscularly as a prophylactic measure 2 to 5 minutes before the initial injection of the anesthetic agent. If subsequent vasopressor activity is required ephedrine, neosynephrin, or desoxyephedrine is given intravenously.

(*c*) *Anesthetic agents.*—For the surgical cases 4 cc. of 1 percent pontocaine hydrochloride are diluted with 6 cc. of 10 percent dextrose so that each cubic centimeter of the mixture contains 4 mg. of pontocaine. The initial dose is from 4 to 16 mg. (average 12 mg.) depending on the physical state of the patient and the operation proposed.

The subsequent doses are usually one-half the initial dose and are administered at 75- to 90-minute intervals or whenever there is increased restlessness, diminution of relaxation, or pain. In several cases where extreme Trendelenburg position is desired by the surgeon a hypobaric solution of pontocaine (0.1 percent) is used. Dilute hyperbaric solutions of procaine are used for the differential spinals in diagnostic and therapeutic procedures.

(*d*) *Supportive therapy.*—An intravenous infusion of 5 percent dextrose in distilled water is administered to all patients before administering the anesthesia. Whole blood is used freely, as needed. Oxygen by nasal tube or mask is given to patients in the older group, and to patients with cardiovascular disease.

ANALYSIS OF CASES

Table 1 shows a summary of cases according to the type of operation performed. The indications for continuous spinal anesthesia were: (*a*) any subdiaphragmatic procedure expected to last longer than 90 minutes; and (*b*) a patient with no contra-indication to spinal anesthesia, but in whom the risk of uncontrollable hypotension following a large "single-dose spinal" would be too great. In our series there was a preponderance (96 percent) of intra-abdominal procedures.

TABLE 1.—*Survey of operations*

Operation	Number of cases	Average age
Subtotal gastrectomy	90	47
Cholecystectomy	40	43
Abdominoperineal resection	21	48
Colectomy	21	45
Exploratory laparotomy	21	48
Colostomy	13	51
Appendectomy	9	43
Intestinal obstruction	8	43
I & D abdominal abscess	8	47
Cholecysto-enterostomy	7	59
Gastro-enterostomy	6	59
Genito-urinary operations	7	35
Orthopedic operations	5	37
Retroperitoneal tumors	3	25
Miscellaneous	16	46
Total	275	46

Of the 275 patients the average age was 46 years; the mode 51 to 55 years; and the range 18 to 80 years. Men comprised 94 percent of the group. Eighty-eight percent were white patients. The weight ranged from 86 to 246 pounds and the height from 4 feet to 6 feet 5 inches.

Of this group 15 patients received continuous spinal anesthesia on 2 separate occasions and 2 patients on 3 occasions.

The duration of the operations varied from 20 minutes (closure of wound evisceration) to 9 hours (pancreatoduodenectomy) with the

average being 2.7 hours. The average number of doses of pontocaine was 2.1. The smallest total dose of anesthetic drug was 4 mg. and the largest 48 mg.

The initial systolic blood pressure varied from 85 to 200 mm. of mercury. Although the fall in blood pressure following subsequent doses occurs as often as after the initial dose, the latter were so small as to require little or no treatment. The blood pressure drops occurred most often at the time of manual abdominal exploration with traction on the mesentery. These were transient unless accompanied by pronounced blood loss. Nausea and retching occurred in about 60 percent of the patients who did not receive general anesthesia and was incidental to visceral traction.

In addition to its use for surgical anesthesia the catheter technique is particularly well adapted for use in certain diagnostic and therapeutic procedures (table 2). Using the ureteral catheter method we performed several differential spinal blocks according to the method described by Arrowood and Foldes (*15*) and Arrowood and Sarnoff (*16*) using a 0.2 percent solution of procaine hydrochloride. These were done as diagnostic aids in the preoperative evaluation of (*a*) patients with hypertension for possible sympathectomy, and (*b*) patients with intractable pain for possible cordotomy. The method was also useful in the treatment of peripheral vascular spasm following vascular surgery and in acute embolic phenomena of the lower extremities in the effort to improve collateral circulation. Following the suggestion of Love (*17*) this method was also used for continuous spinal fluid drainage in the control of pronounced cerebral edema following cranial injury. Using the pulse pressure as a guide it was possible to administer intravenous fluid and simultaneously withdraw spinal fluid so as not to increase cerebral edema.

TABLE 2.—*Use of catheter method for diagnosis and therapeutics*

Purpose	Indication	Number of cases
Diagnostic	Preoperative hypertension test for sympathectomy	3
	To evaluate level for cordotomy in intractable pain	3
	To differentiate peripheral pain from pain of "central fixation"	1
Therapeutic	Sympathetic block for:	
	1. Acute femoral embolus	1
	2. Vascular surgery	2
	3. Anuria due to severe blood transfusion reaction	1
	Continuous spinal fluid drainage in cranial injury	4

SUPPLEMENTAL ANESTHESIA

No attempt was made to rely solely upon the spinal anesthesia. Supplemental agents were used freely to insure maximum comfort for the

patient and to minimize disturbance to the surgeon due to retching and straining by the patient. Table 3 shows a review of the cases according to the supplemental agents used. Some 20 percent were sufficiently quiet following the preoperative medication to require no further hypnosis. Fifty-two percent received intravenous injections of morphine sulfate and scopolamine (25:1 ratio). It was found that these agents were most effective when given a few minutes before excessive abdominal traction was made. Pentothal sodium was given either in 0.5 percent solution by slow drip or in 2.5 percent concentration by small divided doses. A combination of pentothal-nitrous oxide-curare was given in 2 cases where subsequent doses of spinal anesthesia were impossible because of a kink in the catheter, and in 3 cases where the anesthesia failed because the catheter did not enter the subarachnoid space. Cyclopropane was used in 6 percent. Whenever, during the course of the operation, there was severe hemorrhage (4 cases) or shock (1 case) further use of spinal anesthesia was deferred and the operation was completed under cyclopropane-curare. Cyclopropane in small amounts was found to be the agent of choice in controlling hiccups during gastric surgery.

TABLE 3.—*Supplemental anesthesia*

Agent	Indication	Number of cases	Percent
Morphine sulfate and scopolamine.	Sedation and hypnosis	128	52
Pentothal sodium	Excessive restlessness	23	9
	Augment effects of morphine	14	6
	Surgical anesthesia with nitrous oxide and curare	5	2
Nitrous oxide	Analgesia and hypnosis	13	5
Cyclopropane	Surgical shock	5	2
	Hiccuping	3	1
	Incomplete spinal	3	1
	Hypnosis	5	2
None		51	20
		250	100

COMPLICATIONS

Postspinal headache which occurred in 41 cases (16 percent) was the most common complication observed in this series. Our criteria for a postspinal headache were as follows: A headache coming on after spinal anesthesia, different in character from any headaches that the patient might have had previously, which was aggravated in the upright position and relieved in the recumbent position. In 31, the

headache was of less than 5 days duration and in 10 it lasted up to 12 days. The average for the group was 4.7 days. Although it was difficult to evaluate the severity of the headache, 9 were classified as mild, 25 as moderate, and 7 severe. In 2 with most severe headache there was associated meningismus but smear and culture of the spinal fluid failed to reveal any organisms. The fluid did, however, appear xanthochromic.

An attempt was made to determine if any relationship existed between postspinal headache, type of operation, and age of the patient. As table 4 indicates, there was no correlation between type of operation (upper or lower abdominal) and the occurrence of headache (columns 3 and 4). However, it was noted that the younger patients

TABLE 4.—*Headache following continuous spinal anesthesia*

Operation	Number having headache	Percent of total	This operation percent all operations	Average age for operation	Average age with headache
Gastrectomy	15	35	32	47	40
Cholecystectomy	9	22	15	43	38
Small bowel surgery	5	12	8	47	39
Large bowel surgery	1	2.5	15	48	33
Exploratory laparotomy	4	10	8	48	36
Other operations	7	18.5	22	46	46
Total	41	100	100	46	40

were prone to develop spinal headaches. The age mode for the series was 51 to 55 years, but the age mode for patients with spinal headache was 35 to 40 years. Furthermore, the average age of a patient having a particular operation was higher than the average age of the patient having that operation and developing a spinal headache (columns 5 and 6 of table 4). In the group that had multiple continuous spinal anesthesias one patient developed headaches following both and one patient had a headache after the first but not after the second operation.

In our series there were no deaths resulting from anesthesia alone.

In the present series where supplemental anesthesia was used freely, the incidence of pulmonary complications appeared to be the same as in the series of Lemmon and Paschel (*6*) in which no supplemental agents were used.

One patient had total spinal anesthesia following the initial dose (10 mg.). Respiration ceased but she reacted after 45 minutes of artificial respiration during which time her blood pressure and pulse remained normal; the operation was continued. Upon discharge from the hospital she had no apparent ill effects.

Two patients had backache at the site of lumbar puncture not related to trauma during anesthesia. This condition cleared up with-

in a period of 3 months. In no instance did local infection develop at the site of the catheter.

There were two cases of transient residual paresthesia and muscle weakness. In both there was extreme paresthesia at the time of insertion of the catheter through the needle so that the needle was withdrawn and reintroduced at a different interspace. One of these had persistent muscle weakness for about 4 months. The other continued to have hypesthesia and muscle weakness 3 months after the operation, but showed definite improvement with physiotherapy.

FOLLOW-UP

One hundred and seventy-five patients in this series were seen from 2 to 18 months following operation. Of these, 26 have died as a result of primary disease (mostly carcinoma) and 5 of other causes. The remaining patients were well and had no complaints referable to the anesthesia except the patient previously mentioned.

DISCUSSION

The ureteral catheter (Tuohy) technique of administering continuous spinal anesthesia has proved to be a simple, inexpensive method with certain advantages. First, the catheter can be introduced with the patient on a carrier or bed. This makes the method adaptable to many diagnostic and therapeutic measures. Second, the catheter is introduced far enough into the subarachnoid space to insure that it will not be dislodged by movement of the patient. This permits more freedom in handling the patient and gives more certainty of satisfactory anesthesia with subsequent doses.

There are some theoretical disadvantages to the method. First, it is possible to introduce the catheter into the epidural space and obtain inadequate anesthesia. This can be easily recognized by the failure of spinal fluid to drip from the catheter, and can be remedied by reinsertion. Second, the catheter can kink as the patient lies on it, but this is rare if sufficient care is taken to tape it in place properly. Third, the catheter may be sheared off. To our knowledge no such incident has been reported. Fourth, there is an ever-present danger of local infection, but we have seen no evidence of this even in a case where the catheter was in place for 72 hours. Lastly, there is a high incidence of transient paresthesia at the time of insertion of the catheter but there has not been a correspondingly high incidence of residual paresthesia.

The use of light supplemental anesthesia was found to enhance the patient's comfort, and by its inhibition of reflex nerve-impulses makes for smoother operating conditions.

Residual transient paresthesias were encountered in two cases. This has also been reported following the use of the malleable needle by Apgar (*12*) and Hale and Shaar (*14*).

The incidence of postspinal headache was 16 percent in this series. Hale and Shaar (*14*) using the malleable needle technique at this hospital in 1940 to 1943 encountered this complication in 11 percent of their cases. The incidence of headache following "single dose spinal" in this hospital has been 9 percent. Moreover the incidence has been reported as less than 2.5 percent following the use of the malleable needle by Lemmon and Paschel (*6*) (*11*), Apgar (*12*), and Ansbro and Pico (*10*). On the other hand Cann and Wycoff (*18*) using a slight modification of the catheter technique reported headache in 30 percent. It would appear that the incidence of spinal headache following the use of the catheter is higher than with the malleable needle or with the conventional spinal needle. If one of the factors causing spinal headache is the leakage of spinal fluid through the hole in the dura, it would seem that the large hole made by the 16-gage needle would leak more fluid than either of the others which are smaller. Another factor in this higher incidence may be the vigorous early ambulation of recent years which would account for the manifest headaches during the first few days following operation.

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AN EVALUATION OF OXYGEN THERAPY, by Philip B. Price, M. D.; Ralph C. Richards, M. D.; and James B. Hammond, M. D. Annals of Surgery **130:** 747–754, Oct. 1949.

When respiration remains unimpeded in shock, administration of oxygen is of dubious value. Anoxia may indeed be present to a dangerous degree, but breathing oxygen will not correct it. In such cases, time and effort would be better spent in giving blood and blood substitutes and in other measures designed to improve the failing circulation, for that is where the trouble lies. Restoration of an adequate circulation is the surest way—in fact, it is the only way—to correct the anoxia of shock.

In shock produced by hemorrhage, burns, intestinal obstruction, general peritonitis, crushing injuries of the extremities, and histamine injections, administration of 100 percent oxygen did not result in either clinical improvement or increased oxygen consumption.

Likewise, in central circulatory failure produced by cardiac tamponade, it could not be demonstrated that breathing oxygen had any advantage over breathing atmospheric air.

However, when respiration was definitely embarrassed by central depression, tracheal obstruction, prolonged inspiratory resistance, pneumothorax, or constriction of the chest and abdomen, oxygen therapy was of demonstrable value.

These results should not be surprising. In hemorrhagic and traumatic shock the fault lies primarily in deficient blood volume and depressed circulation, not in failure of the blood to be aerated as it passes through the lungs; whereas, in anoxic anoxia the reverse is the case.—*Abstract.*

Cyst of Patent Urachus

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THE patent urachus is a relatively rare condition associated with the urinary tract. It usually remains undiagnosed unless infection of this structure occurs.

Anatomy and embryology.—The urachus is a musculotendinous structure located between the transversalis fascia and peritoneum extending from the apex of the bladder to the umbilicus. It is the involuted upper portion of the normal fetal bladder that has narrowed and formed a ductlike structure lined by stratified squamous epithelium (*1*). It is derived from the ventral cloaca, which, as development progresses, becomes narrow in its apex or upper part to form the urachus. This modified upper extremity of the bladder is not related to the allantois (*2*). Two commonly described features of the urachus are subject to question: (*a*) that it reaches from the umbilicus to the bladder, and (*b*) that a fibromuscular cord is formed by obliteration of its canal. Begg (*2*) has demonstrated that the first statement is incorrect, since only the abnormal urachus even approaches the umbilicus. In reference to the second statement, regardless of the upward extension of the urachus from the bladder toward the umbilicus, the epithelial lining never undergoes complete obliteration. The end result in normal development is as follows: (*a*) The urachus is rarely more than 5 cm. long; (*b*) it extends from the anterior aspect of the bladder wall with its upper extremity fully 11 or 12 cm. below the umbilicus; (*c*) it connects with the umbilicus by either a fibrous cord or diverging strands of fibrous tissue which are derived principally from the adventitia of the umbilical arteries. Distally, at the termination of the urachus in the anterior bladder wall, there is a transverse fold; when the urachus is patent, this structure prevents the entrance of urine into the urachus, even when its open end can be probed or seen with a cystoscope. The majority of instances of urinary drainage from the umbilicus are not instances of urachal anomalies. Rather, they represent a failure of closure of the upper end of

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the bladder caused by lower urinary tract obstruction and are more properly designated vesico-umbilical fistulas.

Incidence.—Cross (*3*), in 1935 collected only 96 cases of cysts from the literature. A true patent urachus, congenital or acquired, had been found only in 3 instances in 15,000 admissions to the Brady Urological Institute. Other urachal abnormalities are more rare. The reported incidence of urachal anomalies is subject to question in many instances because of the improper diagnosis of vesico-umbilical fistulas. Herbst (*4*) found only 148 recorded cases of patent urachus. In 200,000 admissions to the Childrens and Infants Hospital, Boston, Mass., there were 3 cases of patent urachus (*5*). Campbell reported 15 such cases in 12,080 autopsies on children. The ratio of men to women with this condition is 2:1 (*6*).

Pathology.—There are four principal types of urachal anomalies: (*a*) complete (patent throughout from bladder to umbilicus); (*b*) blind external (patent at the umbilical end only); (*c*) blind internal (patent at vesical end only); and (*d*) blind end (cyst, the most common type).

Dudgeon (*6*) listed 8 types of urachal pathology: (*a*) exstrophy of the bladder; (*b*) patent urachus; (*c*) patent urachus and omphalomesenteric duct (4 cases); (*d*) malignancy (45 cases of mucinous carcinoma (*7*)); (*e*) cysts which may weigh as much as 100 pounds; (*f*) abscess (most common); (*g*) calculus (4 cases); and (*h*) tuberculosis (1 case). Pesqueira and Engelking (*8*) reported 1 instance of actinomycosis.

Symptoms causing a patient to present himself for treatment are almost uniformly those associated with infection. Lower abdominal pain and tenderness are the most common complaints. A suprapubic mass with or without drainage from the umbilicus is frequently present. Gastrointestinal symptoms may predominate suggesting that peritoneal involvement has occurred and that perforation into the peritoneal cavity is imminent (*9*). Dysuria and pyuria suggest bladder communication.

The *diagnosis* of urachal disease is not easy. The more important conditions to consider in differential diagnosis are: (*a*) appendiceal abscess; (*b*) ascites; (*c*) ovarian cyst; (*d*) distended bladder; (*e*) pregnancy; (*f*) diverticulitis; and (*g*) patent omphalomesenteric duct (*10*). The diagnosis is established by cystoscopy, cystography, and radiographic demonstration of a tract by injection through an umbilical opening. Roentgenograms to determine the presence or absence of abnormal soft tissue shadows, and the absence of a tract extending intraperitoneally, may assist in definite differentiation (*11*) (*12*).

The *treatment* of urachal anomalies is always surgical. The infected cyst should be incised, drained, and excised later (*13*). Pri-

mary excision is the procedure of choice for large uninfected cysts, malignancy, tuberculosis, and draining urachal fistulas. The added protection of sulfonamides and antibiotics may permit a more radical primary approach than was possible in the past.

CASE REPORT

A 30-year-old officer was admitted to this hospital on 25 December 1948 complaining of fever, mucopurulent drainage from the umbilicus of 4 weeks' duration, and pain and swelling of the lower abdomen of 3 weeks' duration. At the age of 13 years he had frequency of urination and periumbilical pain which subsided without treatment. During the current episode umbilical irrigations with penicillin were given at an Air Force station hospital. These gave temporary relief. With the onset of pain he was given penicillin in oil with no improvement. At no time were there symptoms of bladder irritation.

On admission his temperature was 101° F. The leukocyte count was 10,300 per cu. mm. The urine was normal. The abdomen was moderately distended, voluntary rigidity with severe periumbilical and infraumbilical tenderness was present. There was a moderate amount of foul-smelling purulent discharge from the umbilicus and a probe could be inserted 3 cm. caudad through the small umbilical opening. Four centimeters below the umbilicus there was a tender mass about 5 cm. long but with ill-defined lateral margins. Nonhemolytic *Staphylococcus albus* and *Streptococcus* were cultured from the umbilical sinus. A tentative diagnosis of an infected urachal remnant of the blind external type, or of an omphalomesenteric duct was made.

Intravenous pyelograms were normal. Cystoscopic examination revealed no evidence of a urachal opening. Injection of the umbilical tract with a contrast medium showed a narrow tract extending distally in the midline of the abdominal wall for a distance of 3 cm. ending in a saccule 2.5 cm. in diameter.

Three days following admission the infraumbilical mass was explored. The peritoneal cavity was entered through a right paramedian incision. For a distance of 1 cm. on either side of the midline the peritoneum and omentum were densely adherent to the anterior abdominal wall. The inflammatory mass was continuous with the bladder wall but did not enter the vesical cavity. The mass was removed by sharp dissection including the involved peritoneum, omentum, and umbilicus. Drains were placed in the prevesical space. Closure of the posterior rectus abdominis sheath and transversalis fascia was accomplished with difficulty because about 2.5 cm. of the peritoneum and adjacent structures had been excised. The postoperative diagnosis was abscess of a patent urachus. This was confirmed by pathologic examination.

Both penicillin and streptomycin were administered postoperatively. The course was smooth until the fifth day when the patient, while straining on the bed pan, split the lower portion of the abdominal wound through the anterior rectus abdominis sheath. The wound was closed and the patient was able to take sick leave on the sixteenth postoperative day. Examination 1 month later showed him completely free of symptoms with the abdominal wall well healed.

DISCUSSION

This case represents the most common of urachal anomalies consisting of a cyst of the urachal remnant. The umbilical sinus communicating with the abscess cavity may represent the portal of entry of

infecting organisms. This is in contrast to the pathogenesis of the septic urachal cyst in which the urachus has been ruptured during the normal descent of the bladder, resulting in the liberation of small amounts of urine in the extraperitoneal space. The preoperative secondary diagnostic consideration of an infected omphalomesenteric duct prompted the paramedian incision, which was unsuited to the procedure performed. Without the use of antibiotics, primary excision of the infected cyst involving the peritoneum and secondarily the omentum would have been unduly hazardous. With an established diagnosis, drainage to be followed by excision later is the procedure of choice, particularly in view of the increasing resistance of many organisms to currently employed antibiotics.

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Mesenteric Cyst Complicated By Intestinal Obstruction

Report of a Case

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MESENTERIC cysts are uncommon abdominal tumors. They seldom cause acute symptoms, because of their slow growth and soft consistency. Therefore, it is believed that a case of intestinal obstruction produced by a mesenteric cyst in a 10-month-old infant is worth reporting.

Benevieni is credited with being the first to describe (in 1507) a mesenteric cyst which he noted at autopsy in an 8-year-old boy. Miller (*1*) believes that the cyst found in a young male adult and reported in the same series, more closely fulfills the criteria for mesenteric cysts as we recognize them today.

In 1803, Portal published a classification of these tumors. In 1842 Rokitansky described a chylous cyst which he noted at autopsy. Tilloux in 1880 successfully operated upon one of these cysts, and in 1883 Pean successfully treated one by marsupialization.

Many cases of mesenteric cysts have been recorded and many have been successfully treated by surgery, however, Flynn (*3*) in 1930 still maintained that "mesenteric tumors are among the rarest tumors met with in the abdomen."

A number of theories have been offered to explain the pathogenesis of mesenteric cysts, and numerous attempts have been made to classify them. Ladd and Gross (*4*) suggest that they originate from "misplaced bits of lymphatic tissue" which proliferate, and then fluid accumulates because they do not communicate with the remainder of the lymphatic system.

Guthrie and Wakefield (*5*) point out that it is possible for mesenteric cysts to have their origin embryologically from true diverticula of the small intestine which grow into the mesentery and become pinched

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off; they may be absorbed or else persist and form cysts. They also state that definite proof of their theory "will come when someone is able to find a carcinoma developing in one of these cysts." In 1940 Peterson (*6*) reported an embryonal carcinoma of a mesenteric cyst in a 55-year-old white man.

Many classifications of mesenteric cysts have been offered. Peterson (*6*) divides all cysts of the mesentery into two groups. Under the first or embryonic group he includes: (*a*) Cysts arising from embryonic remnants and sequestrated tissue which include serous, chylous, sanguineous, and dermoid cysts; (*b*) cysts arising by sequestration from the bowel, including Meckel's diverticulum; and (*c*) cysts of urogenital origin.

In Peterson's second group (pseudocysts) are included: (*a*) those of infective origin, hydatids, and cystic degeneration of tuberculous nodes; and (*b*) cystic malignant disease.

Ladd and Gross (*4*) believe that true mesenteric or lymphatic cysts should be differentiated from cysts of enteric origin. They point out that these two types differ both as to their pathological picture and treatment.

The enteric cyst is a thick-walled structure with a serous coat, two layers of smooth muscle, and a mucous membrane lining, while the mesenteric cyst is thin-walled and has no muscular coat or mucosal lining. The wall of the latter consists of connective tissue; in some specimens there is a layer of flattened endothelial cells on the inner surface. These two authors further emphasize that anatomically the musculature of the enteric cysts is intimately associated with that of the intestine, and that its blood supply is the same as that of the adjacent gut. Consequently the enteric cyst cannot be removed without injury to the intestine and destruction of the blood supply of that particular segment. On the other hand, although the mesenteric cyst may lie against the mesenteric surface of the intestine "there is a line of cleavage between the two" so that the cyst can usually be removed without injury to the bowel or its blood supply.

On the basis of content, mesenteric cysts are of two types, serous or chylous. Those containing chylous fluid generally arise from the mesentery of the jejunum, where the material draining from the intestinal tract contains a high percentage of fat. The content of the serous cysts is similar in chemical composition to blood plasma.

Mesenteric cysts have been found in both infants and adults, the oldest reported patients being over 60 years of age (*2*). Incidence is highest in the fourth decade and lowest in the first and sixth. These cysts occur twice as frequently in women as in men (*2*) and occur mainly in members of the white race, although one has been reported in a Chinese boy (*7*).

Clinical symptoms due to mesenteric cysts are extremely variable depending upon the location of the tumor. They occur in any part of the mesentery but the jejunum and ileum are the most frequently involved. Occasionally smaller cysts may accompany the main one and confuse the clinical picture.

Warfield (*2*) has pointed out that these tumors are extremely mobile, especially in the transverse direction because of the nature of the mesenteric attachment, and that pain occurs more frequently than with any other type of abdominal cystic tumor. The size of the cyst and the pressure it exerts on neighboring viscera is another factor which may influence the clinical picture.

In a series reported from the Mayo Clinic (*5*) it was noted that "cysts with less than 2.5 cm. diameter failed to produce any physical signs or symptoms." However, these authors suggest that a sudden hemorrhage into a small cyst or twisting of its pedicle may produce an acute abdominal crisis.

Large cysts though incompletely filled and of soft consistency can, by their "saddle-shape structure" (*4*), compress or strangle adjacent intestine. The picture is that of partial or complete intestinal obstruction with chronic or acute symptoms, no different from those seen in obstruction from any other cause.

Tuberculous peritonitis is the diagnosis most frequently made preoperatively when the cyst produces a painless abdominal enlargement. These tumors are difficult to palpate and demarcate because of their flaccidity. With large cysts it may be possible to elicit a fluid wave.

Roentgenological study, including films of the abdomen, gastrointestinal series, or barium enema, offers more diagnostic aid than any other laboratory procedure. Caffey (*3*) points out that these cysts appear as shadows of watery density displacing the intestines and stomach. Ladd and Gross (*4*) suggest that if roentgenological studies show that the mass lies in front of the intestines, it is more likely to be an omental cyst than a mesenteric tumor.

The most satisfactory treatment of any mesenteric cyst is complete surgical extirpation by dissection from the mesentery. Frequently, because the tumor is widely adherent to an adjacent portion of the intestine, part of the intestine must be excised with the cyst. Marsupialization of the cyst should not be done when excision is feasible.

CASE REPORT

D. S., a 10-month-old white boy was admitted to the hospital 29 May 1948. The mother stated that the child was vomiting, restless, and had had fever for 3 days. In addition the child had had no bowel movement for 2 days.

Birth history and past medical history were irrelevant except for occasional attacks of vomiting of 2 to 3 days' duration and failure to gain weight normally.

Physical examination on admission revealed a thin, dehydrated, white male infant. Admission weight was 17 pounds 2 ounces (normal for age and birth weight, 21 pounds). Temperature was 99.4° F. (rectally). The abdomen was distended, and there was no visible peristalsis. Auscultation revealed an occasional high-pitched peristaltic tinkle.

Rectal examination was negative.

Laboratory examinations.—Red blood cells, 4,200,000 per cu. mm.; hemoglobin, 12 grams; leukocyte count, 7,500 with 40 percent polymorphonuclears, 52 percent lymphocytes, 6 percent mononuclears, and 2 percent eosinophils; urine contained traces of albumin and acetone; plasma chlorides, 460 mg. per 100 cc. blood, and carbon dioxide combining power was 46 volumes per 100 cc.

Roentgenogram of the chest was negative.

Roentgenograms of the abdomen showed dilated loops of small bowel with multiple fluid levels (fig. 1) and a homogenous opacity occupied the entire lower abdomen. This was misinterpreted as ascites or fluid in obstructed bowel.

Figure 1.—Preoperative roentgenogram shows the gas-filled obstructed small intestinal loops crowded into the left upper abdomen by the cyst which is represented by the shadow of watery density which fills the remainder of the abdominal cavity (postoperative interpretation).

Clinical diagnosis.—Small bowel obstruction, etiological factor undetermined.

The patient was intubated and parenteral fluids were administered. After adequate preoperative preparation an exploratory laparotomy was performed on 30 May 1948.

Operation.—Under open-drop ether anesthesia, the abdomen was entered through an upper right rectus incision. On opening the peritoneum a small amount of serosanguinous fluid escaped and dilated loops of small intestine appeared in the wound. A large flaccid, multilobulated cyst with a milky white glistening wall was readily delivered from the abdomen by shifting its fluid content and causing it to "flow" through the incision.

The cyst arose from the mesentery of a loop of small intestine and presented from both sides in dumbbell fashion. The central constriction in the cyst was produced by a tightly stretched compressed overlying bowel, the proximal loop of which had undergone torsion. A band of devitalized gut about 1 centimeter wide was present at the site of obstruction.

The small intestine, both proximal and distal to the cyst, was divided between clamps. The lesion and overlying bowel were exercised by wedge resection of the involved mesentery. This cyst was located approximately at the junction of the jejunum and ileum.

The divided ends of small bowel were inverted and a side-to-side anastomosis was performed. The rent in the mesentery was closed, the short proximal stump of intestine was turned in against the mesentery, and the abdominal wound was

A B

Figure 2.—A. *The anterior aspect of the cyst shows the undilated loop of small intestine distal to the obstruction appearing as a constricting band around the cyst as the latter protrudes from either side of the mesentery;* B. *Indicates area of intestinal obstruction.*

closed in layers. Silk sutures were used throughout. Convalescence was uneventful.

Pathologist's Report

Gross.—The external appearance of the cyst is shown in figure 2. The cyst weighed 650 gm. and its mean diameter was about 14 cm. The wall of the cyst was approximately 1 mm. in thickness. The interna was smooth without papillary folds. The content was milky and not coagulated.

Microscopic.—The cyst wall was composed of a single layer of flattened endothelial cells resting on a supporting wall of fibrous and elastic connective tissue (fig. 3). There was edema in some areas of the cyst wall with a moderate degree

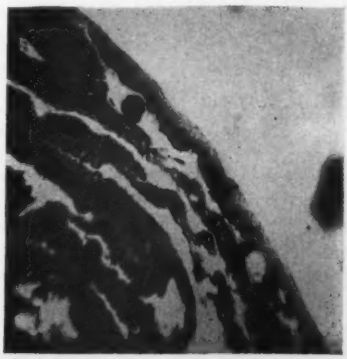

Figure 3.—*A low-power photomicrograph showing the layer of flattened endothelial cells lining the cyst.*

of vascularity. The blood vessels in some areas were dilated and contained laked blood cells.

Diagnosis.—Findings are compatible with a diagnosis of lymphatic cyst of the mesentery.

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Rendich and Harrington reported three cases of mesenteric thrombosis, in two of which they postulated a diagnosis of mesenteric thrombosis. In a patient with a clinical diagnosis of intestinal obstruction, a roentgenogram of the abdomen showed gaseous distention of the small intestines and the right half of the large intestine, suggesting mechanical obstruction in the splenic flexure. Surprisingly the barium enema passed the site of the obstruction to fill the entire colon. This patient died and necropsy showed thrombosis of the superior mesenteric artery with gangrene of the small intestines, cecum, and part of the ascending colon, the regions corresponding to the distribution of superior mesenteric vessels. Harrington reported 4 additional cases with similar roentgenographic signs in which the diagnosis of mesenteric thrombosis was confirmed either at operation or necropsy.

This simple roentgenologic procedure offers a means for differential diagnosis in an acute abdominal surgical emergency where only early and prompt diagnosis will avert an otherwise inevitable catastrophe.—*Abstract.*

Cavernous Hemangioma of the Left Lobe of the Liver

Report of a Case

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ROBERT H. HOLMES, *Lieutenant Colonel, MC, U. S. A.*[1]

SMALL, asymptomatic cavernous hemangiomas are more common than is generally believed. Such small hemangiomas are a frequent incidental finding at autopsy. Large hemangiomas are less common, and rarely does such a lesion attain the size of the one noted in this report.

CASE REPORT

The patient was a 46-year-old Negress who had lived for the past 23 years in Panama. On 22 January 1949 she delivered her thirteenth child in Colon Hospital. Following delivery she noticed a nontender mass the size of an orange, deep in the left upper quadrant of her abdomen. She was discharged from the hospital to return later for further investigation of the mass. She returned in May. In the 4 months' interval the mass had increased in size and occupied most of the upper abdomen. A barium enema and gastrointestinal series were normal except for the displacement caused by the tumor. Numerous consultants examined the patient and concluded only that she presented a rapidly enlarging mass, apparently of a cystic nature. An exploratory laparotomy was performed on 22 July. A mass involving the left lobe of the liver was found, with sharp demarcation between an apparently normal right lobe and the tremendous tumor involving the left lobe. A biopsy was reported as a cavernous hemangioma of the liver. After an uneventful recovery the patient was transferred to the Gorgas Hospital.

On 11 August the abdomen was again opened through a long right rectus incision. A few dense adhesions had developed between the vascular mass, abdominal wall, and adjacent jejunum. After the release of the adhesions, this unusual tumor was found to measure 42 by 28 by 22 cm. and contained an estimated 1,000 cc. of blood. The left lobe of the liver was indistinguishable from the mass, and it appeared that the tumor was the greatly enlarged left lobe of the liver. The tumor occupied the entire left side of the abdomen and its lower pole extended below the brim of the pelvis. The distinction in appearance between the normal right lobe and the left lobe of the liver was so clear as to form a semblance of a pedicle. The hepatoduodenal ligament was incised and a careful dissection of the hepatic artery was accomplished. The right hepatic artery was identified and traced to the right lobe of the liver, and

[1] Gorgas Hospital, Ancon, C. Z.

a greatly enlarged left hepatic artery was traced to the tumor. The important adjacent structures were identified and found to be beyond the limit of the intended transection of the liver. Accordingly the left hepatic artery was doubly ligated and severed. Next, the left triangular ligament was severed, additional adhesions were released, and the left lobe was mobilized.

During this procedure the tumor was held out of the abdomen, and it was observed to decrease in size, to about half its original dimensions. It appears that with the left hepatic artery ligated, the patient was, in effect, given an autotransfusion from the tumor. The liver was quickly transected at the junction of the right and left lobes. Hemorrhage was controlled by digital compression. The larger intrahepatic vessels were individually ligated. Hemostasis was completed by inserting a series of interrupted mattress sutures of heavy silk. Convalescence was uneventful. The patient was discharged on the twentieth postoperative day. Frequent follow-up visits since that time indicate an apparent cure.

Pathologist's Report

Gross findings.—The large, encapsulated, red-brown mass measured 21 by 15 by 6 cm. and weighed 1,050 gm. The capsule was thin and transparent. One surface exhibited a suggestion of a pedicle measuring 3 by 4 by 1 cm. The mass was soft and spongy, but fibrous on cutting revealing a bloody meaty parenchyma. Two large fibrous trabeculae traversed the mass and radiating therefrom were many smaller, interlacing septums (fig. 1).

Figure 1.—Cut surface of hemangioma of liver. Note wide, fibrous supporting trabeculae and monotonous bloody, spongy architecture.

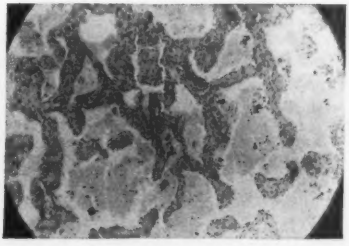

Figure 2.—Cavernous blood sinuses in juxtaposition with islands of liver cells and thickened anastomosing septums of blood sinuses.

Microscopic findings.—Multiple sections showed anastomosing vascular channels of variable size lined by elongated flattened cells resembling endothelium. Most of the sinuses contained blood. Occasional islands of liver cells were observed within this mosaic. There was a monotony of pattern with little cellular pleomorphism (fig. 2).

Diagnosis.—Cavernous hemangioma of liver.

DISCUSSION

In 1904 Albrecht (*1*) introduced the term "hamartoma" for certain vascular tumors of the liver which he considered to represent a malformation or developmental defect. This defect appeared to express itself as an abnormal combination of normal components of the organ, and could be one of arrangement, quantity, or degree of differentiation.

This concept and terminology has since been employed by many authors.

Multiple hamartomas have also been reported. Von Falkowski (*2*) described an infant exhibiting nodules of vascular tissue in the liver, the spleen, and multiple angiomas of the skin. Turner (*3*) reported a case of arterovenous hamartoma of the brain. Moolten (*4*) pointed out that neurofibromatosis was possibly an instance of disseminated hamartoma. The existence of combined hemangioma of the cerebellum and retina is well established. Recently one of us saw two cases of congenital familial telangiectasia with multiple vascular lesions of the skin, mucous membranes, and a large pulmonary arteriovenous fistula. In one of the lungs four additional small hemangiomas were discovered. McDonald, Harrington, and Clagett (*5*) reported 23 cases of pulmonary hamartoma. Numerous cases of hemangioma involving bone are recorded. Congenital polycystic disease of the liver, kidneys, and pancreas is also quite familiar. Tuberous sclerosis is also incriminated in this galaxy of developmental tumors.

The relationship of the frequent cutaneous hemangiomas, apparently unrelated to visceral involvement, to the concept of Albrecht's hamartoma needs clarification. These vascular tumors wherever found are usually benign although instances of malignancy have occurred. Kaposi's metastasizing angiosarcoma if related to the hamartoma must represent a malignant mesenchymal variant. Stout (*6*) rejected many cases of supposed malignant vascular tumors. Most vascular tumors cannot be differentiated from hamartomas, or vascular malformations, the apparent tumor being caused by non-neoplastic enlargement of preexisting vascular tissue (*7*). Jaffe (*8*), Taylor and Moore (*9*), and De Navasquez (*10*) suggest that metastasis in certain cases is only apparent, being actually of multicentric origin. True malignant tumors of vascular origin are extreme rarities (*11*). Hastings-James (*12*) reported a fatal case of hemangioblastoma of the liver. The present case is concerned with a huge apparently benign hemangioma of the liver that was successfully removed. The history is somewhat alarming in that the mass grew to the size exhibited in about 6 months. The presence of an intact capsule and an accessible pedicle facilitated complete removal.

Gruenwald (*13*) pointed out that the age at which a disturbance takes place has often been considered as a criterion for malformation and birth has been set as the borderline, but he could not subscribe to this assumption since identical malformations may develop before and after birth. A disturbance of embryonic growth indicates a structural mutation with the factor of differentiation and rate of growth altered but not uncontrolled and the quality of function partially maintained. A disturbance of growth, such as cancer, in

postnatal or adult life, on the other hand, usually implies an anatomic, functional, possibly genetic mutation with the quality of differentiation regressive or lost, and proliferation uncontrolled. It is suggested that the hamartomas embrace features of both extremes. A hamartoma, therefore, is a developmental defect manifested by an overgrowth of tissue yet responsive to organized influences, exhibiting the quality of specific structural and functional differentiation as well as controlled rate of growth and benign natural history. The present case represents these features and as such can be considered a hemangio-hamartoma. The mechanism of formation can be explained as a disturbance of a mesenchymal vascular anlage, of unknown etiologic basis, but possibly heredopathic (*14*).

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Benign Esophageal Stricture and Carcinoma of the Esophagus[1]

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UNTIL 1941 only 31 cases of carcinoma of the esophagus arising at the site of chronic strictures of that organ had been recorded. In that year, Benedict (*1*) critically analyzed these cases and added 2 of his own. A review of this group reveals that 17 of the strictures followed lye burns, 2 resulted from foreign bodies, and 1 was congenital. The remaining 13 were "unknown" or of unreported causation. In the case to be presented, no background factor of known significance could be elicited. Of special interest is the youth of the patient.

CASE REPORT

A 38-year-old white veteran was admitted to the Halloran Veterans' Administration Hospital on 13 May 1948 with a history of acute esophageal obstruction of 3 weeks' duration. Dilatation at another hospital had been only partially successful and obstruction had recurred.

Past history.—At age 12, he had an episode of sudden esophageal obstruction requiring gastrostomy and repeated bouginage. After 1 month, dilatation was effected to the point where the gastrostomy was permitted to close.

The following years were uneventful until 1944 when he entered a station hospital in France for "battle fatigue." At that time he complained of some difficulty in swallowing large boli of food. Roentgenogram showed a stricture of the upper one-fourth of the esophagus. In 1945 he was honorably discharged from service and continued his occupation (bakery wagon driver) until the present illness.

With the exception of evidence of recent weight loss (24 pounds) the physical examination was negative. Laboratory examinations were as follows: Hb., 14 gm. per 100 cc., 5 million red blood cells per cu. mm., 8,000 white blood cells per cu. mm., and a normal differential. The stools were repeatedly negative for occult blood. The urinalysis was negative; the blood proteins, 6.8 gm. per 100 cc. with a normal A/G partition. The esophagram showed at the junction of the proximal and middle thirds of the esophagus, practically obstructing the lumen, an irregular ragged defect, 4 cm. in length, and several dentate projections, sug-

[1] Sponsored by the Veterans' Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are a result of his own study and do not necessarily reflect the opinion or policy of the Veterans' Administration.

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Figure 1.—Gastrotracheal fistula at necropsy

gesting sinuses arising from the left lateral wall of the lesion. Esophagoscopic examination showed a fungating tumor, 19½ cm. from the upper incisors and biopsy showed the growth to be a squamous cell carcinoma. Bronchoscopic examination was negative.

Under endotracheal ether-oxygen anesthesia, a subtotal esophagectomy with intracervical gastro-esophageal anastomosis by the Sweet technique (*2*) was performed by the consultant in chest surgery.[3] No local metastases were detected and the 7½ hour operation was completed without untoward incident. The carcinoma, which measured 3 cm. in length, almost completely obstructed the lumen and penetrated to the outermost layers of the esophageal wall.

On the fifth postoperative day the patient was up and around and eating a soft diet. With the exception of transient discomfort substernally when he overate, he had no complaints and during the following 3 months he did remarkably well. There was a weight gain of 15 pounds but a persistent irritative cough appeared which became aggravated on swallowing food. Bronchoscopic examination in August 1948 showed an extension of the carcinoma into the trachea just above the tracheal carina. High voltage roentgen therapy was given without beneficial results. Jejunostomy was performed but the course was progressively downhill and the patient died 2 months after the latter procedure.

At necropsy a 3.5 by 2.5 cm. perforation of the stomach into the trachea, approximately 4 cm. below the level of anastomosis (fig. 1), and metastases were present in the paratracheal region as well as in the right posterior chest wall and right visceral pleura.

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[3] Dr. W. Chamberlain.

Sound Problems in the Air Force

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HORACE O. PARRACK, *Ph. D.*[1]

THE operations incident to the manufacture, test, and flight of aircraft have always been noisy. The noise problem became so acute during World War II, particularly because of the adverse effects of noise on speech communication, that a great deal of effort was expended by both governmental and private laboratories in: (*a*) devising methods for suppressing noise generation (*1*); (*b*) designing sound-absorbing and sound-excluding treatments for the interior of aircraft (*1*) (*2*) (*3*); and (*c*) designing and constructing noise-excluding devices to be worn by personnel exposed to noise (*4*) (*5*).

Baranek (*6*) (*7*) discusses the effect of noise on comfort and safety in residential structures and has suggested possible solutions to these problems. Knudsen (*8*) in a more general discussion of noise as a hazard to safety, efficiency, and comfort has presented data on typical noise levels in streets, transportation facilities, work areas, and residential areas. He proposes the following as standard "Acceptable Noise Levels."

In hospitals	35 to 40 decibels.
In private offices	40 to 45 decibels.
In factories	45 to 80 decibels.

The operation of conventional aircraft, both on the ground and in flight, is accompanied by sound levels in excess of the proposed "acceptable" maximum for factories (*9*). With the development of the jet power plant the noise levels have been greatly increased.

Various complaints, attributed to high frequency sound, have been and are being received from men who test and service jet engines and from pilots of jet propelled aircraft. From men working with jet engines on the ground, these complaints have included deafness; tinnitus; vibration of the head, teeth, abdomen, and chest; nausea; vomiting; unusual fatigue; and increased irritability both on the

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job and after hours. Pilots' complaints included acute fatigue, inability to concentrate, headaches, loss of flying "feel," numbness and detachment while flying, and sensations of faintness. This article deals with some of the known relationships of air-borne sound to the problems of supersonic speeds and sound of ultrasonic frequency.

Sound in the ultrasonic frequency range means sound at frequencies above the audible frequency range. The American Standards Association (*10*) has tentatively adopted the arbitrary range of 15 to 15,000 cycles per second (double vibrations per second) as the frequency limits of audible sound. While this seems to be a good generalization, many children and young adults with "perfect" ears can hear sound frequencies as high as 20,000 cycles per second and when the tones are loud enough some people can hear frequencies at least as high as 25,000 cycles per second (*11*) (*12*) (*13*). To what extent do such high frequency sounds exist? Every time one vocalizes a loud "pssst" many measurable ultrasonic frequencies are produced. Compressed air escaping from a jet on the laboratory bench is an excellent source of ultrasonic frequencies.

Since the war microphones capable of measuring this high frequency sound have been developed and many such measurements made (*14*). Figure 1 shows the results of measurements made near a jet engine. Here sound pressure is plotted as a function of frequency. Immediately it is apparent that ultrasonic frequencies are present

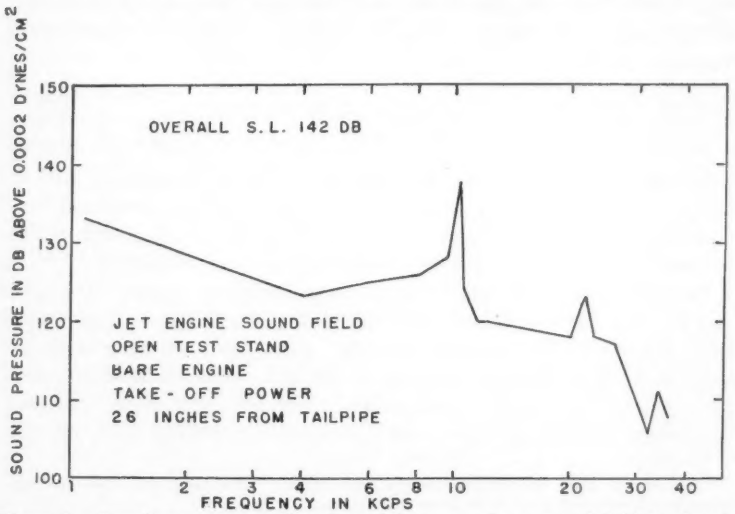

Figure 1.—Sound pressure as a function of frequency for a sound field produced by a turbo-jet engine (high frequency analysis, 400 cycles per second half-band width).

and that they are low in intensity compared to the audible sound frequencies present. To the best of our knowledge these are the highest sound levels in the ultrasonic frequency range that have been recorded either around jet engines or in jet aircraft. Sound in the audible frequency range at levels up to 120 decibels above the standard reference does not appear to be injurious to man except for effects on or through the hearing organ.

Does sound pitched too high for the human ear to hear in some mysterious way penetrate the body and cause damage of some sort at rather low intensities? As far as air-borne sound is concerned, such is not the case. These frequencies are almost totally reflected by the skin. Measurements of the sound reflection and absorption coefficients at various frequencies have been made for white rats and for man (*15*). For the white rat about 5 percent of the sound energy is absorbed at 400 cycles per second. This absorption drops to about 2.5 percent at 1,200 cycles per second and then rises to about 12 percent at 6,000 cycles per second. If the rat's fur is shaved off, the sound absorption again is 5 to 7 percent of the total sound energy present for a frequency of 400 cycles per second and this absorption decreases rapidly with increasing frequency until it is only 0.5 percent at 3,600 cycles per second. The absorption coefficient of rat fur alone has been shown to be about 1.5 percent at 400 cycles per second and increases with increasing frequency to about 7.5 percent at 3,600 cycles per second. Above 1,200 cycles per second the absorption coefficient for the fur alone is identical with that for the intact animal. We have no reason to believe that the absorption decreases again until much higher frequencies are reached.

When such furred animals as mice (*16*), rats, and guinea pigs (*17*), are placed in sound fields of the order of 155 decibels above the standard reference level the fur and body temperatures rise to lethal levels in very short times. Exposure of rats to radiant heat under appropriate conditions has caused death in approximately the same time, has brought about an essentially identical behavior during exposure, and has produced essentially identical pathologic changes. One must conclude that the absorption of acoustic energy from the sound field with conversion to heat and elevation of the body temperature is the primary cause of death.

At this point it might be well to point out that the decibel scale is logarithmic and that sound energy in a sound field that contains no standing waves or reflections increases as a square of the sound pressure. Thus an increase of 20 decibels means a tenfold increase in sound pressure and a hundredfold increase in sound energy. Or for another example, at 126 decibels the sound pressure is approximately twice and the sound energy four times their respective values at 120 decibels.

If we were to expose one of these animals to a sound field just three decibels less intense than one which would just kill him, he will be exposed to and absorb only one-half the lethal quantity of sound energy and should be able to reach a stable equilibrium with his environment. Experimentally this has proved to be true (*18*). The animal's temperature rises to 37° to 38° C. and becomes stable at that point. Following exposure to such a sound field for an hour or more the animal appears to be deaf but continues in good health in all other respects indefinitely. Thus it is clear that even the rat with his highly absorbent fur coat can survive quite well in sound fields of the order of 150 decibels above the standard reference.

Now man is not a rat and he does not normally wear a fur coat. The sound absorption coefficients for man vary with frequency as they do for a shaved rat except that they are even lower (*15*). At a frequency of 400 cycles per second man's skin absorbs about 4.8 of the total sound energy. The absorption coefficient decreases rapidly with increasing frequency until it is less than 0.5 percent at 6,000 cycles per second and even less at 18,000 cycles per second. The difficulties of measuring such small absorption coefficients are such that it is impossible to give exact figures. At the present time there is no reason to believe that this absorption coefficient rises at even higher frequencies. Men exposed to ultrasonic frequencies produced by a siren in the laboratory at levels 40 decibels higher (100 times the sound pressure and 10,000 times the sound energy) than have been found around jet engines have noticed no ill effects. It thus becomes highly improbable that air-borne sound in the ultrasonic frequency range, even at higher intensities than we have found to exist anywhere but in the laboratory, will be harmful to man.

This would seem to contradict much of the work and many of the statements appearing in the literature on the subject of ultrasonics. For many years small crystal ultrasonic generators have been used to disrupt bacteria and micro-organisms, to accelerate chemical reactions, and to produce destructive lesions in laboratory animals (*19*) (*20*) (*21*) (*22*) (*23*). Horvath (*24*) (*25*) (*26*) in Germany and Herrick (*27*) in this country at the Mayo Foundation have been investigating the use of such ultrasonic generators in the treatment of cancer. In all of this work contact between the crystal generator and the exposed material was made through an oil or water medium from which air had been carefully excluded. Under these conditions surface reflection phenomena are minimal and nearly all of the sound energy generated by the crystal is absorbed in the exposed biological material thereby heating or otherwise disrupting the structure. The conditions for ultrasound in air are quite different. Sound energy at high frequencies in air is almost completely reflected by any liquid or

solid surface. Much of the confusion concerning ultrasound as an Air Force hazard arises from the mistaken inference that the results obtained with fluid-coupled generators are valid for air-borne sound. They are not.

The bulk of the aeromedical sound problem is thus confined to the audible sound frequencies. Figures 1 and 2 show that sound levels in excess of 130 decibels may be expected from a few hundred cycles per second up to 10 or 12 thousand cycles per second. At some frequencies the level may be as high as 140 decibels with this particular engine, and with more powerful engines we have found the sound level to be as high as 150 to 160 decibels.

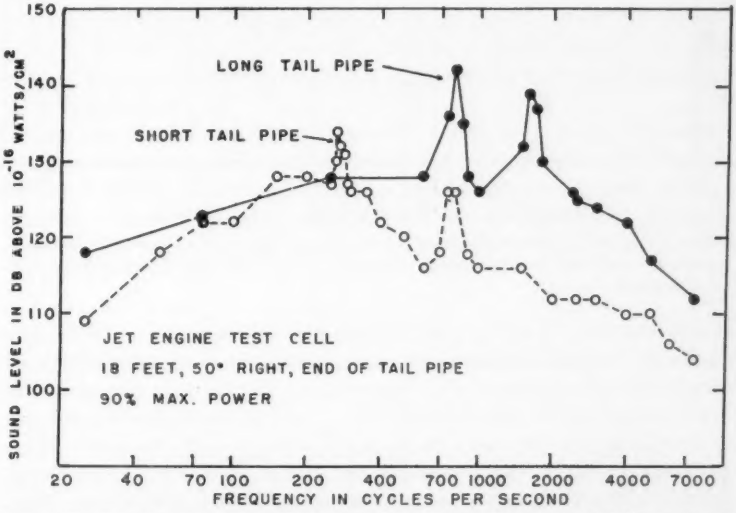

Figure 2.—Sound pressure as a function of frequency for a sound field produced by a turbo-jet engine (low frequency analysis, constant percentage band width, down 3 decibels at 1 percent of tuned frequency).

Obviously the ear is of first importance when considering sound in the audible frequency range. At about 120 decibels most persons feel a tickling or uncomfortable sensation in the ear. The threshold for pain in the ear varies with individuals, but most will feel pain by the time sound levels have reached 140 decibels (*28*). Judging from a single case where rupture of the drum occurred in a known sound field, one can expect rupture of the drum to occur at a sound level of about 160 decibels (*29*).

Davis et al. (*30*) have shown that significant temporary hearing losses will occur after exposure to pure tones or to band spectrum noise for 4 to 8 minutes at levels of 120 decibels above the standard reference. By temporary deafness we mean a deafness that follows

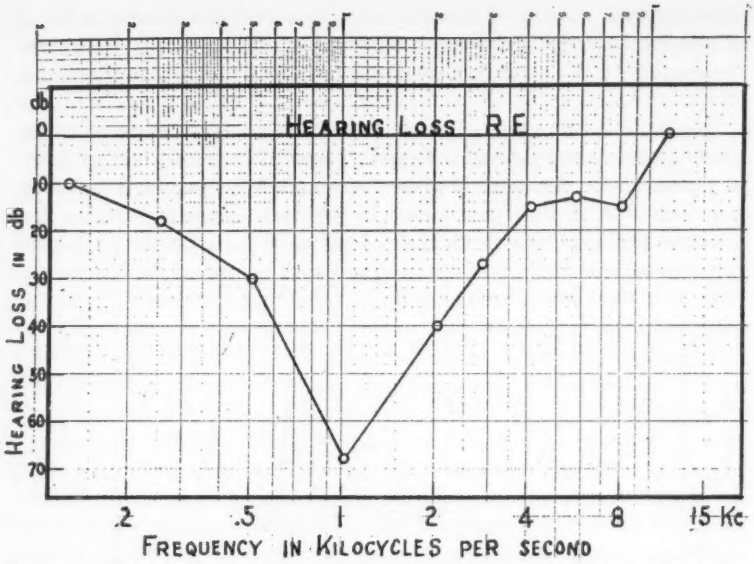

Figure 3.—Hearing threshold loss as a function of frequency following a 10-minute exposure without ear defenders to jet engine noise at 146 decibels above the standard reference level.

overstimulation, is not permanent, and is apparently due to fatigue of the end organ. Longer exposures at intensities of 110 decibels or shorter exposures at intensities higher than 120 decibels will give similar hearing losses. Since a jet engine will produce sound pressures at least as high as 130 decibels throughout the speech frequency range (300 to 4,000 cycles per second) it seems obvious that the unprotected ear will suffer from exposure to such noise. Figure 3 shows the hearing loss that existed 12 minutes after an ear had been exposed for 10 minutes, without ear defenders, to a 146-decibel over-all sound level near the exhaust of the jet engine whose sound field is presented in figure 1. The hearing loss is in excess of 30 decibels throughout the frequency range 500 to 2,000 cycles per second. This is the most significant frequency band for the perception and understanding of speech.

During the last war considerable effort was directed toward providing means of protecting the ears of men who fired guns, operated tanks, flew in aircraft, worked in factories, and tested engines. In most cases, where continuous noise was encountered, the sound level was less than 125 decibels. The result of this effort (*4*) (*5*) was the V–51R ear defender, a small insert-type ear plug made of either vinylite or neoprene. When various factors such as size, weight, comfort, chemical and physical irritation of the external canal, available

materials, et cetera, are considered, it seems that the V–51R excludes sound from the ear about as well as an insert-type defender can do. Under optimal conditions of fit the V–51R provides:

26 decibels sound attenuation at 100 and 250 cycles per second.
29 decibels sound attenuation at 500 cycles per second.
31 decibels sound attenuation at 750, 1,000, and 1,500 cycles per second.
35 decibels sound attenuation at 2,000 cycles per second.
36 decibels sound attenuation at 2,500 to 8,000 cycles per second.

For sound levels up to 125 decibels it can be seen that the V–51R is reasonably adequate protection, reducing the sound level at the ear to less than 100 decibels. Using this same sound attenuation data, it can be calculated that at a frequency of 1,000 cycles per second and an intensity of 140 decibels the sound level at the ear would be reduced only to 110 decibels. Davis et al. (*30*) have shown that sizable temporary hearing losses may be produced by a 1,000-cycle per second tone at 110 decibels.

The hearing loss shown in figure 4 resulted from an incidental exposure to a "synthetic" sound field and demonstrates these limitations of the V–51R. The sound field was generated by a laboratory siren inside an anechoic room. Standard V–51R ear defenders, carefully fitted to the subject's ears were worn throughout the exposure. The

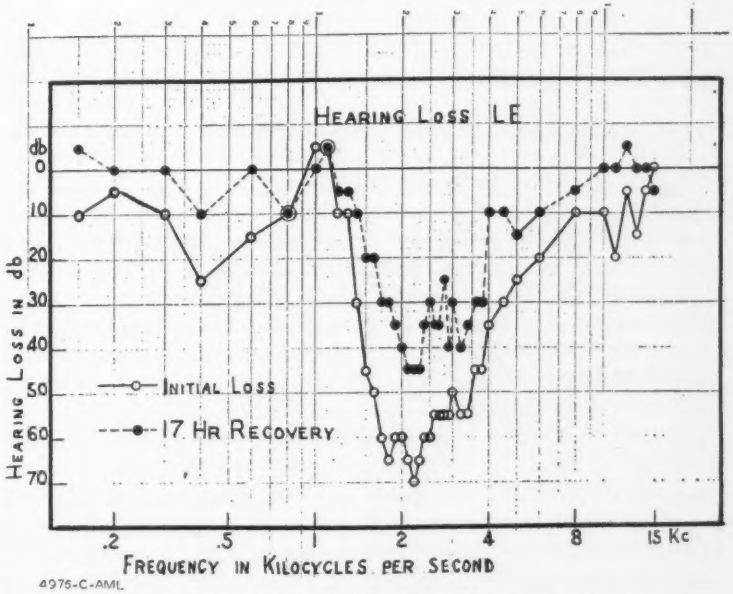

Figure 4.—Hearing threshold loss as a function of frequency following exposure to siren sound field.

sound field has been labeled "synthetic" because the exposure consists of two consecutive exposures each to a different fundamental frequency generated by the siren. The frequencies, the exposure times, and the sound levels are as follows: (*a*) 1,300 cycles per second for 60 minutes at levels of 130 to 157 decibels; and (*b*) 2,700 cycles per second for 28 minutes at levels of 135 to 157 decibels. Note the extensive hearing loss between 1,500 and 4,000 cycles per second. Note also the small amount of recovery that occurred in 17 hours. Under similar conditions we have encountered one loss of 90 decibels from 1,200 to 1,500 cycles per second following a 45-minute exposure to 1,000 cycles per second at 130 to 156 decibels.

Further protection for the ears can be obtained by using ear muffs in addition to insert-type ear defenders. The Standard Air Force Intermediate weight flying helmet with doughnut-type (AN–48440–1) earphone sockets represents one such device which has been designed especially to exclude noise. These earphone sockets under optimal conditions of fit and snugness provide (*31*):

5 decibels sound attenuation at 100, 250, and 500 cycles per second.
11 decibels sound attenuation at 750 cycles per second.
18 decibels sound attenuation at 1,000 and 1,500 cycles per second.
22 decibels sound attenuation at 2,000 and 2,500 cycles per second.
27 decibels sound attenuation at 3,000 cycles per second.
34 decibels sound attenuation at 4,000 cycles per second.
45 decibels sound attenuation at 5,000 to 10,000 cycles per second.

If the acoustic insulation of the V–51R were added to that of the helmet, under optimal conditions of fit we might expect nearly 50

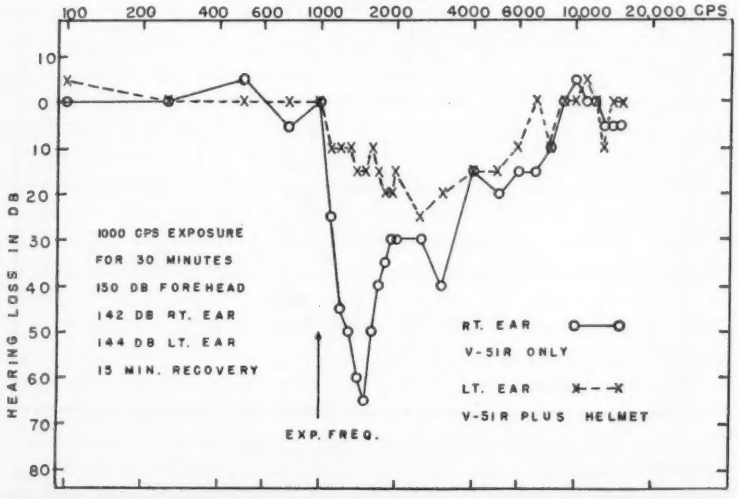

Figure 5.—Hearing threshold loss as a function of frequency following exposure to 1,000 cycles per second siren sound field with two methods of ear protection.

decibels protection at a frequency of 1,000 cycles per second. Figure 5 shows the hearing loss produced by an exposure to a tone of 1,000 cycles per second at 142 to 150 decibels when both ears were protected by V–51R ear defenders and the left ear was further protected by the helmet earphone and socket. These curves approximate quite closely the hearing losses that these particular ears show after exposure to a 1,000 cycles per second tone for 30 minutes at 95 and 110 decibels respectively. The loss shown by the right ear compares favorably with the losses found by Davis et al. for a 32-minute exposure to a 1,000 cycles per second tone at 110 decibels.

The combination of the V–51R plus some kind of ear muff as provided in a Standard Air Force helmet does provide adequate ear protection for periods as long as 30 minutes in sound fields up to 145 decibels. Further protection in the form of personal equipment seems useless for several reasons. First, at higher sound levels than this, bone conduction of sound to the ear can be expected to be sufficient to produce significant hearing losses. The nearly 50-decibel attenuation given by this combination at 1,000 cycles per second represents approximately the difference between air and bone conduction. In fact we are not sure but that bone conduction played some part in producing the small loss shown for the doubly protected ears. Any personal equipment which could be designed to protect against bone conduction of the sound to the ear would be too cumbersome to wear while working. Secondly, sound fields of 145 decibels or more have been found uncomfortable and annoying for parts of the body other than the ears.

The relation of the temporary deafness to permanent deafness is still an open question. During the past 9 years one man working in this field has sustained many severe temporary hearing losses with no audiometric indication of permanent damage to his ears. The only precaution observed was that complete recovery to his normal threshold audiogram be allowed between such exposures. Since this recovery may take several days one might postulate that repeated daily hearing losses without sufficient time for recovery to normal might have produced a permanent loss.

MacLaren and Chaney (*32*) in a study of 5,000 audiograms obtained on employees of an aircraft manufacturing company present data which indicate the development of permanent impairment to hearing as a result of exposure to factory noise. The percentage of employees having audiograms interpreted to be indicative of deafness produced by "acoustic trauma" increased with increasing noise levels. A smaller group of employees, selected because of their audiograms were considered characteristic of deafness resulting from "acoustic trauma," were provided with ear defenders which were worn while

in the noise field. After 3 days considerable recovery occurred but at the end of 30 days there was very little more recovery of auditory sensitivity and the hearing threshold was still appreciably depressed. This hearing loss may be permanent. In addition many cases were found where the total hearing loss increased steadily as shown by audiograms taken over a 6- or 12-month period. It appears probable that those persons who exhibit progressive hearing loss with increasing time of exposure to noise will be permanently deaf as a result of the repeated "acoustic trauma."

In addition to the temporary deafness and possible permanent deafness previously discussed, the ear is subject to masking of desired speech or code signals by undesired noise. Any sound is said to produce masking when it raises the threshold of audibility of a second sound (*33*).

The effectiveness of a sound as a masking noise depends about equally on its frequency components and its intensity (*34*). Of course, if the desired signal is as loud or louder than the noise, it can be heard. Also if the masking noise is louder than the desired signal but contains only frequencies much lower or higher than the desired signal, the signal will be heard. Although one can talk and be understood through the noise of hammering or the 75 to 150 cycle per second noise produced by a reciprocating engine with a propellor, it is much more difficult to do this in the presence of noise produced by rubbing two pieces of sandpaper together or in the presence of the hiss of aerodynamic noise.

It is usually accepted by pilots that the B–25 is a very noisy airplane and that the F–80 is a very quiet one. It is true that in the frequency bands from 20 to 300 cycles per second which contain the engine and propellor noise, the sound levels of 110 to 115 decibels inside a sound-treated B–25 (*11*) are 6 to 13 decibels higher than they are in an F–80. However, in the frequency bands from 300 to 4,800 cycles per second the sound levels in the F–80 (*35*) of 112 to 114 decibels are 9 to 22 decibels higher than they are in the B–25. While the lack of very low frequency sound and vibration in a jet aircraft and the noise excluding properties of helmets give the pilot and crew the impression it is a quiet airplane, direct speech communication is nearly impossible due to the high level masking noise in the speech frequency spectrum. It is indeed fortunate that helmets and headsets with doughnut type seals are much better for excluding noise in this frequency range than they are for excluding propellor noise.

It has been pointed out that while sound frequencies above 6,000 cycles per second are very poorly absorbed by human skin, 4 to 8 percent of the sound energy may be absorbed at lower frequencies. For frequencies below 2,000 cycles per second, intense sound of the

order of 150 decibels becomes a problem for parts of the body other than the ear. Using a laboratory siren generating sound levels between 150 and 170 decibels some interesting phenomena have been observed in man at these low frequencies (*17*). At frequencies from about 1,500 cycles per second down to about 700 cycles per second there is a sensation of marked vibration of the cranial bones. At certain of these frequencies the sensation of vibration from the jaw is so strong that one reflexly grits his teeth in an effort to stop the vibration.

There is also a sensation of vibration combined with air movement in the nasal passages and bony sinus. A similar sensation is noted in the mouth and pharynx, especially when the mouth is open. At certain frequencies, which have not been precisely determined, in the range 700 to 1,500 cycles per second, the vision may become blurred when one stands in the sound field. Recovery is immediate and complete as soon as one steps out of the sound field. As the frequency of the sound field to which one is exposed is still further decreased, the sensations of vibration are felt in the thorax, abdomen, and in single muscles or muscle groups of the arms and legs.

The sensations of vibration that have been observed in the laboratory at known frequencies and intensities of the sound field are identical with sensations observed when standing near the tail pipe of a jet engine on an outside test stand. Where standing wave patterns may be produced in enclosed test cells these phenomena are more distinct.

There have been occasions both in the laboratory and at jet engine test stands when personnel have observed a "weakness" in the knees or an apparent general weakening of the body supporting musculature. This sensation is usually not accompanied by faintness or vertigo. It would appear to result from some effect on the proprioceptive reflex mechanism, since, with conscious effort, one can maintain his posture and move about. At higher sound levels in this frequency range a few subjects have experienced vertigo in addition to the weakness described. During short exposures none of these vibratory sensations are accompanied by pain or after effects so that it is doubtful that gross physical damage occurs. Yet even experienced observers feel considerable discomfort and apprehension in these sound fields. Such loud low frequency sounds instinctively mean danger to a man. After exposures of 30 minutes or so fatigue, irritability, and a feeling of being slightly drugged have been observed. So far the modes of action and physiologic changes which accompany these reactions have not been adequately studied. Due to the bulkiness and weight of materials that would be required to insulate a man from such sound and vibrations, structural sound

insulation rather than personal equipment seems to be the practical approach for any protective measures necessary.

In the case of engine test facilities much progress has been made along this line. However, experience has shown that even well-designed and well-insulated control rooms and work areas fail to exclude sound when workmen fail to close windows and doors or fail to seal up the space around fuel and control lines running between control rooms and the engine test bed.

In conclusion it can be stated that sound above the audible frequency range is not currently a serious hazard. The knowledge of the existence of such sounds and in some cases the presence of annoying sounds in the upper audible frequency range may be psychologically disturbing to some persons. However, three major sound problems do exist. The first is the problem of deafness, both temporary and permanent. By the use of both insert-type and external ear defenders adequate protection may be expected in any sound field that is not so intense or so low in frequency as to be disturbing to the body as a whole. The second problem is the one of masking of speech in communication systems. Sound insulation for these frequencies is not too difficult and appropriate headphone and microphone design can be expected to provide satisfactory solutions. The third problem is the intense low frequency sound which is felt by the body as a whole. To date the only solutions seem to be spatial isolation and/or structural isolation in the form of engine mufflers and sound-proofed buildings.

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Medical Plans for Civil Defense and Disaster Relief[1]

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IN THIS brief presentation it is hoped that we may achieve orderly thinking and make concrete suggestions of use to local and State committees in planning the medical phase of civil defense and disaster relief. Without a great deal of forethought, prolonged training, and the development of systematic performances, drills, and tests of all participants, no community can prepare itself to provide those additional health services that will be essential for civilians subjected to disasters. When the average community prepares itself for disasters the effort of each citizen and every profession must be fitted into a coordinated system. Whoever guides each part of the whole must have a clear concept of the working of all other parts. There is no easy road to medical preparedness for disasters.

There are two opinions as to local disaster planning. One maintains that no local planning is justified until an authoritative central agency is established to prescribe a uniform pattern for each locality. Such a regimented approach, if implemented, would result in a speedy realization of the desired total readiness. Certain elements of local plans would depend on such a system if mutual support between communities were to be achieved with maximum economy and efficiency. Such a system is the only one likely to survive major war disasters. A second group, maintaining that every community should proceed immediately with its own preparations for meeting disasters, is more realistic. Such a plan would not interfere with any national scheme to be devised later. Each community can lay the necessary groundwork in interim plans and at the same time improve its own and others' readiness to meet many problems that may never require intercommunity participation. Above all, much time and effort can be saved because such planning will be required with or without a uniform national pattern.

Several States and communities have already set up their own flexible schemes, readily adaptable to mutual support or national partici-

[1] Condensed from an address presented at Joint Meeting of Third Army Area Medical Department Reserve Officers and Fulton County Medical Society, Ga., 20 October 1949. Full text available on request to the Surgeon General, Department of the Army, Washington 25, D. C.

pation. None of them should find undue difficulty in adjusting to a future national pattern. No community should go so far in its plans as to provide greater reserve stocks of litters, ambulances, and medical supplies than could be readily used. On the other hand, no community can justify prolonged ignorance of its immediately available resources or neglect the writing of simple, feasible plans and instructions that may be implemented with a reasonable prospect of success. Even if an ideal national plan were produced overnight, it would not permit formation of unchanging national or local plans. Since in the development of any local, State, and national plans it is inevitable that changes will be necessary from time to time, delays to prevent later changes of local plans to meet national schemes will never be justified. This discussion deals with interim plans, that may be reasonable pending the advent of a national plan.

Certain essential activities in an interim disaster medical plan, if not previously considered, should be undertaken without further delay and generally in the following order: (*a*) Fixing responsibilities for all necessary activities;[2] (*b*) establishing necessary authority for meeting these responsibilities;[2] (*c*) classifying responsibilities and authorities as already adequately covered or not; (*d*) providing means for developing services not adequately covered;[2] (*e*) keeping a record of functions to be performed; and (*f*) developing a system of reporting every person treated.

As indicated above, legislation may be needed to fix responsibility, insure proper authority, and provide the means for additional civilian health activities required for disaster relief or civil defense. In civil defense this should be limited to organized civilian activities (*a*) to minimize the effects of any enemy action directed against the United States or other area which is a responsibility of the United States, and (*b*) to maintain or restore those facilities and services that are essential to civilian life, and are affected by such enemy action. A disaster will be considered to be a situation in which numbers of persons are plunged into helplessness and suffering and as a result may be in need of food, clothing, shelter, medical care, and other necessities of life. In disaster relief planning, therefore, the following premises should prevail:

1. Civilians should control and implement all civilian health services.[3]

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[2] May require legislative action.

[3] Under existing law, civil administration could call for temporary military aid to the civil authority. The Hopley Civil Defense plan recommended certain military responsibilities, including final reliance on the Army for support in the event civil efforts were overwhelmed or became exhausted. That must not occur, but if it should the civil administration must be reestablished as soon as possible. To do otherwise might result in diversion of military medical resources from primary missions. The measure of our efficiency would be the speed with which the civil administration could be reestablished.

2. All responsibility to a military or civilian community for functional results rests on a military commander or a civilian administrator, respectively.[4]

3. Military participation may take one or more of several forms: (*a*) Following a disaster, if the civil administration continues to operate, the Army may provide supplemental assistance, usually in the form of medical supplies or food; (*b*) following a natural disaster in peace or war the Army may provide medical supplies, sanitary aid, and other supportive measures as requested by the Red Cross or the States, and always with legal sanction; (*c*) under conditions of martial law, civil laws are administered by a military commander; (*d*) under conditions of military government the commander, subject only to the laws of war and to the instructions of his own civil government, prescribes such measures regarding health as he deems necessary, depending on the recommendations of technical advisors.

4. The functional planning and administration of your programs must be integrated by respective heads of civil and military administrations, to achieve which we must insure that: (*a*) local military and civil administrators are thoroughly familiar with the scope and limitations of their functions; (*b*) those authorities comprehend the relationships that must exist between them, as well as with their respective superiors; (*c*) civil administration will be reestablished as soon as possible; and (*d*) civilians will function under civil control, with minimum military supervision or interference.

In developing community relief services not adequately covered their quantity and quality will depend on the location and type of disaster encountered. The community to furnish the relief services and the organizations responsible for specific functions must be clearly understood. An estimate of potential situations must have been made to permit provision of means (table 1). The categories and quantities of resources required must have been determined (table 2).

Since the limiting factor in any plan will be sufficiently trained personnel to perform the necessary functions, an inventory of available personnel is one of the earliest requirements (table 3). For this purpose personnel in public health services, in teaching institutions, and in any of the regular or reserve and civilian components of the Armed Forces must be considered unavailable. Specialists certified by the American specialty boards should be listed separately. With this information available, we may allocate geographically personnel to all public health, general medical, and specialist team functions.

[4] This is proper, for health officers have authority derived through the military commander or the civilian administrator. On the other hand, the health personnel must make certain that each administrator has made all necessary arrangements for the health services.

TABLE 1.—*Potential situations requiring interim medical plans for civil defense and disaster relief*

[Prepared by Col. William L. Wilson, M. C., U. S. Army, © September 1949]

Community or place of disaster or event	Community to furnish initial relief health services	Community requiring services	Source for additional health services when own are overwhelmed	Community to furnish teams for services	Community in which services may need to be provided
Own only	Own	Own only	Own expanded	Own	Own.
			Own improvised	Own	Own.
			Another community	Own+Others	Own+Others.
Other only	Other	Other only	Other expanded	Other	Other.
			Other improvised	Other	Other+Own.
			Other+Ours	Other+Ours	Other+Own.
Own+Other	Own+Other	Own+Other	Own+Other expanded	Own+Other	Own+Other.
			Own+Other improvised	Own+Other	Own+Other.
			Own+All others	Own+All others	Own+All others.

TABLE 2.—*Preliminary estimate of situation (interim) in medical plans for civil defense and disaster relief*

CATEGORY OF RESOURCES REQUIRED BY CIVIL DEFENSE AND DISASTER RELIEF HEALTH SERVICES

(*Excess to usual, normal requirements*)

1. Hospital facilities.
2. Convalescent facilities.
3. Personnel.
4. Transport.
5. Medical equipment and supplies.
6. Blood and blood derivatives.
7. Food, clothing, feeding, hygiene and sanitation, insect and rodent control, and non-medical equipment and supplies.
8. Medical administration for disaster or incident period.

RESOURCES REQUIRED TO BE PREPLANNED AND ALLOCATED

To category of employment of resources	To category of services required (units and teams to be organized)	To category of special management (for response following disaster or enemy attack)	To zone of activity (from center outwards—even beyond city limits)
1. Casualties services. Medical care and therapy made necessary solely by enemy attack or disaster. (Some qualitative increase of normal services, but primarily mass treatment instead of individual treatment must be organized.)	1. Treatment of wounds: a. Routine (cleansing, antisepsis, antibiotics, anesthesia, analgesia). b. Shock (resuscitation, medication, blood or blood derivatives). c. Hemorrhage (blood and derivatives). d. Infections (prophylaxis and definitive treatment). e. Flesh wounds (immobilization, hemostasis, suturing). f. Burns (mass treatment of physical, chemical, and radiologic burns). g. Vascular injuries (hemostasis, suturing, and repair). 2. Treatment of chemical casualties. 3. Treatment of radiologic casualties. 4. Treatment of neuro-psychiatric casualties. 5. Preventive and therapeutic handling of contamination and contaminated persons, whether casualties or not (radiologic, bacterial, viral and chemical). 6. Evacuation (first aid, aid stations and litter squads). 7. Ambulance (drivers and attendants).	1. Hospitals. 2. Preventive and public health services. 3. Records and reporting. 4. Medical regulating service to control flow of patients. 5. Unit (team) organization, training, equipment and testing. 6. Allocation and assignment of units and persons to: a. Geographic areas of city. b. Type of service to be performed. c. Exact place of duty. d. Offices controlling them. e. Periods of duty. 7. Allocation of equipment and supplies. 8. Procurement, storage, maintenance, issue and distribution of equipment and supplies. 9. Provision of medical transport. a. Control of flow (regulating service). b. Ambulances c. Supply vehicles. 10. Provision of blood and blood derivatives. 11. Mass health services (preventive measures, particularly in mass evacuation, migrations and war displacements).	1. Initial self-aid and first aid. 2. Litter squad. 3. Collecting-aid post. 4. Ambulance. 5. Secondary (clearing) hospital. 6. Base (general) hospital. 7. Convalescent hospitals, and homes. 8. Mutual support from: a. Red Cross. b. Other communities. c. Other states. d. Armed services. e. Others.
2. Preventive and public health services. Made necessary solely by enemy attack or disaster. Primarily quantitative increase of normal services but more vigilance, speed, improvisation, mobility, sustained effort and courage are required as well as a completely organized epidemiologic service.			

TABLE 3.—*Sample inventory of personnel—interim medical plans for civil defense and disaster relief*

[Prepared by Col. William L. Wilson, M. C., U. S. Army, © September 1949]

Medical personnel	In public health services	In school faculties	Unavailable in armed services reserves	Available (less specialists) (A) by Zone of City (C)			
				NW.	NE.	SE.	SW.
Physicians (A)							
Dentists							
Nurses—Graduate							
Pharmacists							
Veterinarians							
Sanitarians							
Dieticians							
Physical therapists							
Nurses' aides							
Practical nurses							
Trained orderlies							
Laboratory technicians							
X-ray technicians							
Other technicians (B)							
Untrained orderlies							
Laborers							
Nonmedical but essential personnel:							
Administrative							
Housekeeping							
Engineering							
Utilities							
Services							

NOTES:

(A) Does not include specialists certified by American boards. These should be listed separately by board specialty and by same categories as shown for physicians to permit allocations to duties.

(B) Includes dental laboratory, dental, dental hygienist, meat and dairy inspection, pharmacy, medical equipment and maintenance, veterinary, optician, orthopedic mechanic, surgery, and all other technicians and technically trained aides.

(C) Where each is major part of every day.

Medical matériel resources should be listed according to whether they are used in public health or medical-care services. Few, if any, changes to normally effective public health services will be required except for quantitative expansion unless it is for additional functions to minimize casualties from atomic, biologic, psychologic, and chemical warfare. Table 4 indicates a method for inventory of immediately available hospital beds. In a similar manner the interim plan must include inventories of medical supplies (table 5) and medical transport (table 6) required for public health, therapeutic, and evacuation services.

The administration of a disaster relief plan requires detailed recording of functions to be performed. We have touched all too lightly on fixing responsibilities and providing authority, and essential means. These must be recorded and sufficiently disseminated to all concerned. Written notice of appointment should be sent to persons responsible for (*a*) preparation and maintenance of all plans; (*b*) procurement and assignment of personnel; (*c*) budgeting, procuring and disbursing funds; (*d*) establishing, publishing, supervising, and controlling policies, procedures, training programs, and training guides; (*e*) publishing operational systems and functions; and (*f*) activating, organizing, administering, and training functional units, such as first-aid personnel individually or in squads; litter-bearing squads; casualty-collecting teams; casualty clearing stations; ambulance drivers, attendants; shock treatment teams; blood and blood derivatives services; general surgical, orthopedic, maxillofacial, thoracic, neurosurgical, abdominal, and vascular surgical teams; burn treatment teams; chemical casualty treatment teams; radiologic casualty treatment teams; psychiatric and psychologic teams; infectious disease treatment teams; and epidemiologic teams. The exact components of these teams have not been prescribed. The organization of such teams in this interim period not only does not need to be uniform, but by their diversity and varied effectiveness will provide valuable experimental information tending to result in the most efficient types.

For interim planning the necessary medical equipment, supplies, transport and other material means should come from normal supply sources. Local efforts to standardize equipment within a community or between mutual-support communities should not be undertaken until national direction has been furnished. There must be written plans and instructions, based on the material inventories, for the procurement, storage, issue, replenishment, repair, and maintenance of (*a*) hospital plant facilities, (*b*) medical equipment and supplies, (*c*) patients' food and feeding, and (*d*) medical transport in the form of medical personnel-carrying vehicles, cargo vehicles, ambulances, and other patient-carrying vehicles.

TABLE 4.—*Hospital beds immediately available in sample city for disaster relief*

Quarter of city	Name of hospital		Address	Number of beds in hospitals with adequate space				Number of beds in improvised hospitals		Total
	Base (full surgery)	Secondary (clearing)		In regular daily use	Not in regular use but ready for emergency		Total with emergency beds	Normal use of space	Source of beds	
					In hospital	Elsewhere				
Northwest	City		4th and Main	900	200	[1] 100	1,200			
		Doaks	9th and Locust	165	10		175			
		Mercy	1425 Grand	150			150			
	St. Thomas		Lee and Front	900	50	[2] 25	975			
		Charity	16 High St	175	20	[3] 5	200			
		Jackson Academy	High and Front					School dormitory 150	School	
		Tom's warehouse	Union square					Dry storage 300	University dormitory (3 miles).	
Subtotal	2	5		2,290	280	130	2,700	450		3,150
Northeast	Wesley		2215 Main	450			450			
Subtotal	1			450			450	0		450
Southeast										
Subtotal	0			0			0			0
Southwest	Maternity	University	Elm and Pearl	70	5		75	Dormitory 700	University	
Subtotal	1	1		70	5		75	700		775
Total	4	6		2,810	285	130	3,225	1,150		4,375

[1] City warehouse.
[2] Staff quarters.
[3] Nurses' home.

TABLE 5.—*Sample inventory of medical supplies—interim medical plans for civil defense and disaster relief*

[Prepared by Col. William L. Wilson, M. C., U. S. Army, © September 1949]

Listing by item required	Available at all times in city	Required				Shortages				Sources for making up shortages	Time required to provide for shortages
		NW.	NE.	SE.	SW.	NW.	NE.	SE.	SW.		
Blood and derivatives											
Drugs, biologic products, and antibiotics											
Surgical dressings and bandages											
Surgical instruments, instrument sets, and aid kits											
Shock team equipment											
Laboratory supplies											
Dental supplies (emergency)											
X-ray supplies											
Miscellaneous hospital and medical supplies											
Sanitary supplies											
Others											

TABLE 6.—*Sample inventory of medical transport—interim medical plans for civil defense and disaster relief*

[Prepared by Col. William L. Wilson, M. C., U. S. Army, © September 1949]

Vehicles required for movement of patients and medical material	Number available at all times in city	Number required				Shortages to be made up			
		NW.	NE.	SE.	SW.	NW.	NE.	SE.	SW.
Motor ambulance									
Motor truck:									
Van									
Large cargo									
Small cargo									
Motor bus									
Other vehicles									
Litters									
Blankets									
Splints and vehicle aid kits									

A scheme for hospitalization and evacuation of patients must be prepared, published, and understood by all concerned. Hospitals provide the basis for the whole system, so a hospital plan similar to that shown in figure 1 may be set up initially. After being tested by drills and experience, changes may be readily made to fit local conditions. As hospitals receive patients and approach capacity performance, provision must also be made for moving convalescent or well patients to other facilities or to their homes. A sample hospital evacuation scheme is illustrated in figure 2. The control of the flow of patients must be assured by establishing a medical regulating office for sections of the city, for the whole city, and for the State. The handling of patients from the application of first aid to their return to normal duties is shown in figure 3.

A records and reporting system referable to every person treated in civil defense or disaster relief must be developed and established in every instance in which the usual medical and health records and reporting will not fully meet requirements. The public must be brought to cooperate by wearing indestructible identification tags. Thus, a casualty, even though unable to talk or furnish self-help could be identified, his family notified, his property rights protected and later his insurance, compensation, or pension rights established. Each civilian medical unit must maintain a register of cases treated.

SUMMARY

Civil defense and disaster relief require the early assignment of responsibilities to persons throughout this scheme for: (*a*) directing, controlling, and supervising operations; and (*b*) coordination between their respective units and all others, particularly for mutual support.

Local civil defense and disaster relief plans must be integrated with military plans by means of (*a*) a simple classification of the entire adult population with regard to physical and temperamental fitness for essential duties in an emergency; (*b*) developing standards of the minimum of health services that would suffice, thereby insuring proper priorities in allocating personnel and matériel; (*c*) inventory of civilian medical resources, using terms that would make comparison between civilian and military resources easily understandable; (*d*) obtaining uniformity in classification of health personnel and in their organization into units of a type that would be equally adjustable to civil or military administration in wartime, could be transferred from one control to another with facility, and could be used with economy and efficiency by either; and (*e*) indexing our aggregate medical and health resources. The matter will be difficult, but can be achieved by cooperation and diligent study on the part of all concerned.

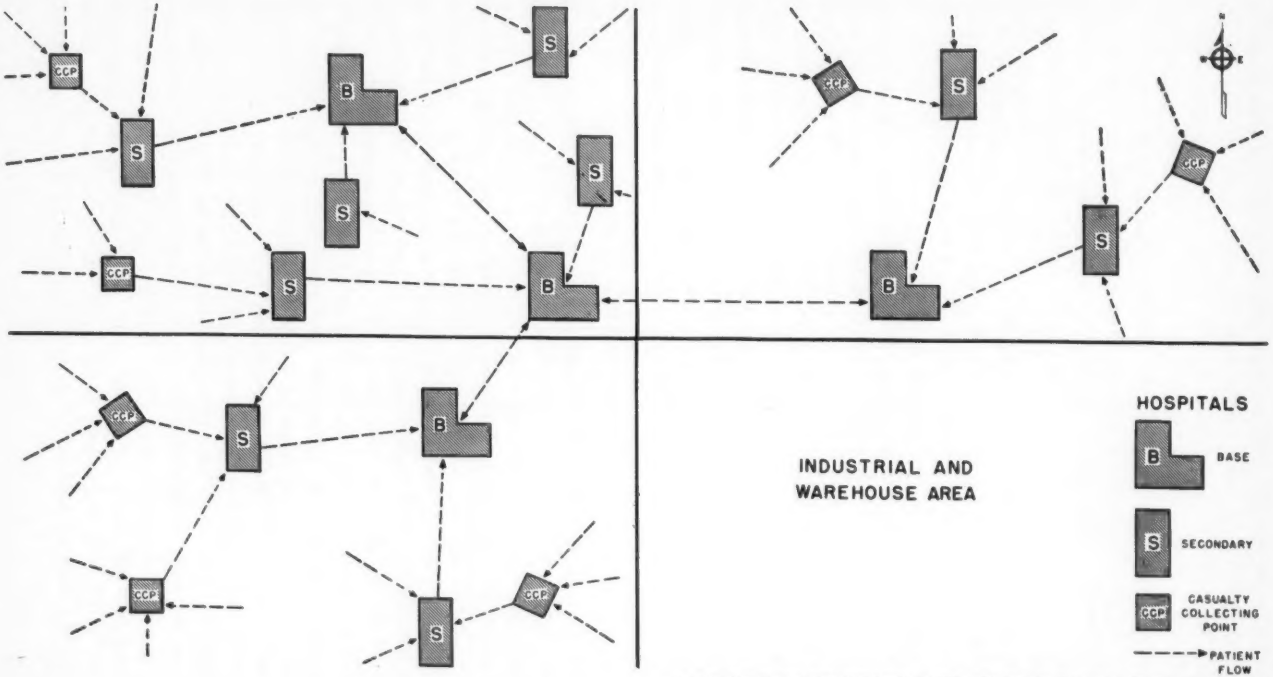


Figure 1.—Sample city. Hospital plan for disaster control.

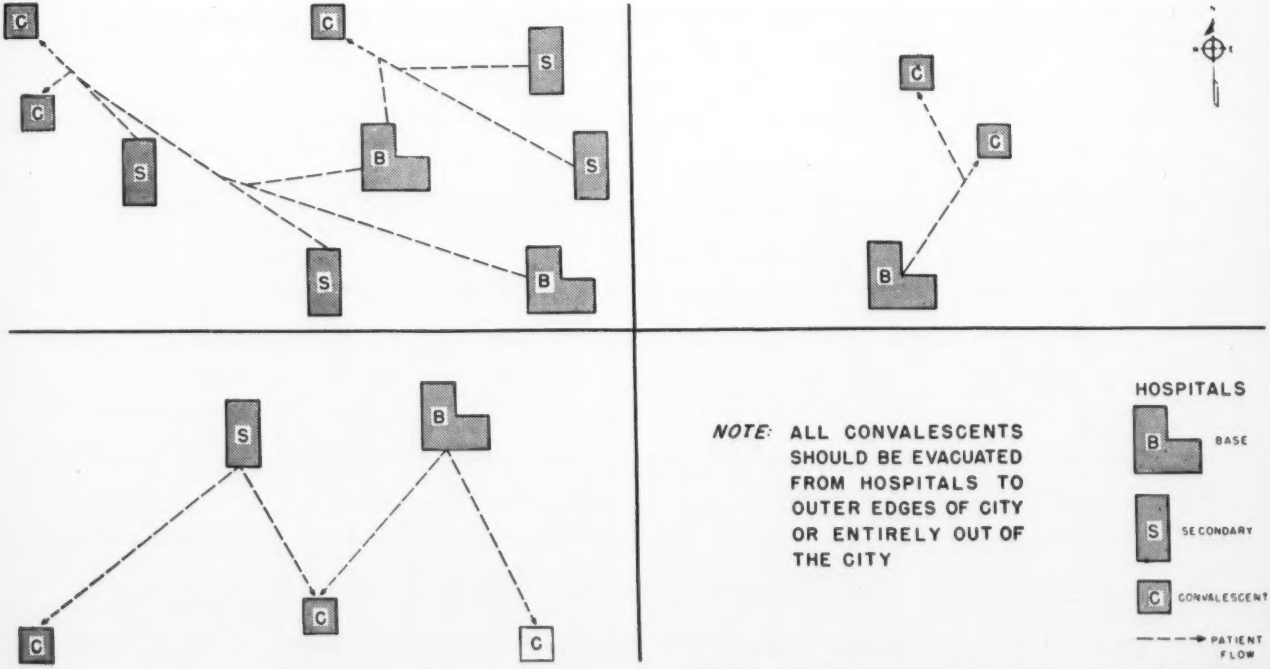
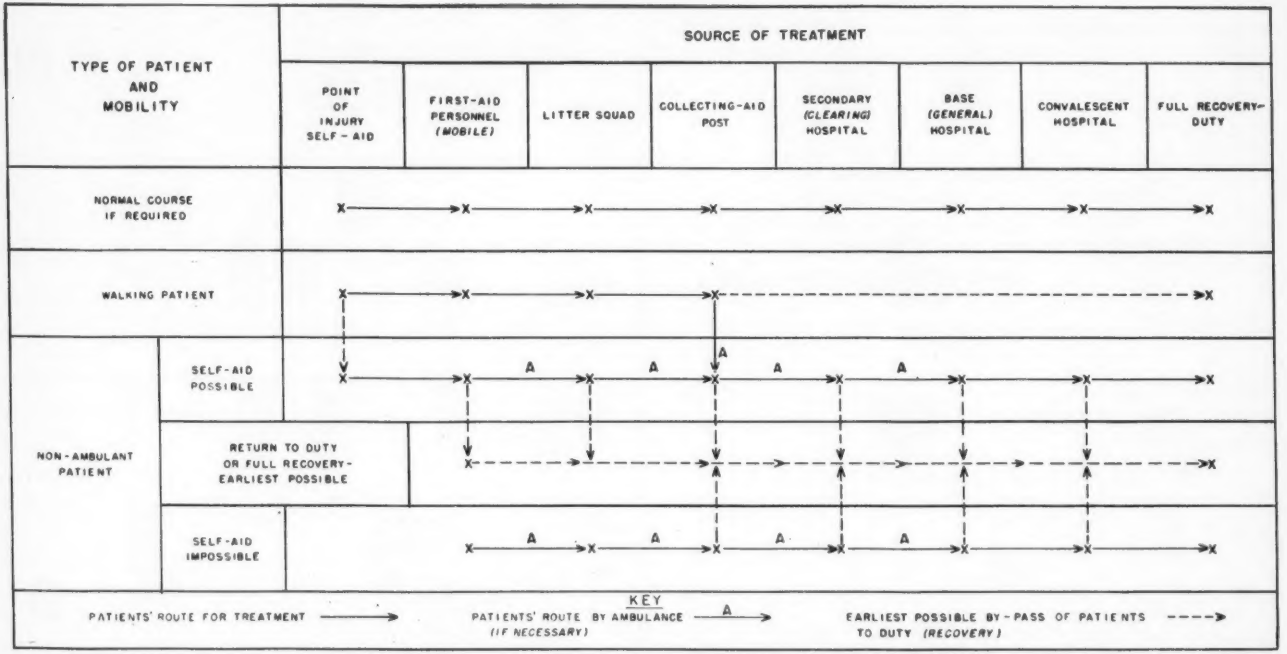


Figure 2.—Sample city. Hospital evacuation of convalescent patients.



—PREPARED BY COL. WILLIAM L. WILSON, MC, U. S. ARMY. © SEPTEMBER 1949

Figure 3.—Medical plans for civil defense and disaster relief—interim evacuation scheme for casualties (diagrammatic).

Although many communities would avoid planning for disasters which might never occur, because the vast efforts we have discussed would be deemed needless and wasted if a nation-wide program of civil defense and disaster control were set up and no disaster ever occurred, we should be happy rather than disappointed.

CHLORAMPHENICOL IN THE TREATMENT OF INFECTIOUS DISEASES, by Joseph E. Smadel, M. D. American Journal of Medicine 7: 671–685, Nov. 1949.

Chloramphenicol is one of the important recent additions to the antibiotics of proved clinical value. It is effective against a wide variety of infectious agents, notably the rickettsiae of epidemic typhus, murine typhus, scrub typhus, Rocky Mountain spotted fever, rickettsialpox, and Q fever. Members of the psittacosis-lymphogranuloma venereum group of viruses, which are now classified as rickettsiae, were also considerably inhibited by this antibiotic. Since chloramphenicol is rickettsiostatic rather than rickettsiocidal, suppressive doses must be given long enough for the patient to develop immunity if he is to remain asymptomatic when the drug is discontinued. Chloramphenicol also has an inhibitory effect on the growth of a wide range of bacteria. The gram-negative bacteria predominate. While inhibition of growth of staphylococci and streptococci is obtained, the concentrations required to affect these organisms are far in excess of the effective concentrations of penicillin. High concentrations of the drug in certain culture media reduced the number of *Endamoeba histolytica*. Of greater significance, however, was the observation that large doses of the drug produced an appreciable clearing of infection in rats and dogs with experimental amebiasis.

Resistant variants can be developed from a number of species of bacteria that were originally susceptible to chloramphenicol. No drug-resistant strains of rickettsiae have yet been developed. Chloramphenicol is extremely stable. The drug levels in serum, urine, spinal fluid, milk, and bile can be determined by bio-assay. The chemical method for determining the drug may be used on serum and spinal fluid, but not on urine. Chloramphenicol is a specific therapeutic agent against typhoid fever. Although it is superior to the earlier forms of treatment for brucellosis, aureomycin appears to be equally efficacious. In the treatment of gonorrhea chloramphenicol compared favorably with other methods of therapy but cannot be relied on to suppress a concurrent syphilitic infection.—*Abstract.*

Streptomycin in the Treatment of Tuberculous Lymphadenitis

JOHN A. C. GRAY, *Commander (MC) U. S. N.*[1]

IN THE large and growing literature on the treatment of tuberculosis with streptomycin, there are few references to the use of the drug in tuberculous lymphadenitis. This is probably due to the fact that scrofula is no longer a common disease. In the seventeenth century King Charles II is said to have administered the "king's touch" to 10,000 cases annually in London (*1*). Yet in a recent series of 3,998 admissions for tuberculosis to the New York City Municipal Sanatorium, Otisville, N. Y., there were only 19 (0.005 percent) patients with the disease; and in 1945 at Bellevue Hospital, New York, only 5 percent of pediatric tuberculous admissions, and only 20 (0.007 percent) of adult tuberculous admissions had tuberculous lymphadenitis (*2*). Nevertheless, though uncommon, the disease is of importance to the patient and to the physician, and an assay of the value of streptomycin in its treatment is appropriate.

It is the purpose of this article to present the results of streptomycin treatment in seven cases of tuberculous lymphadenitis showing what the drug did and did not accomplish.

Tuberculous lymphadenitis is a phase of the systemic disease tuberculosis. The classical concept of scrofula is one of cold abscess following cervical lymphadenitis. This was upset in 1826 when Cruveillhier (*3*) recognized pulmonary tuberculosis as "scrofula of the lungs," and today it is recognized that tuberculous lymphadenitis is inseparable from any manifestation of the disease, be the chief clinical manifestation pulmonary or extrapulmonary. The diagnosis of tuberculous lymphadenitis, therefore, does no more than state that the chief clinical localization is in the lymphatic system. It is recognized that at all times, tuberculosis is a disease involving the entire body, actually or potentially.

When tuberculosis occurs in a lymph node, a portal of entry is necessary. This may be any of the body orifices, including the ocular

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conjunctiva, the skin (*3*), or the dental roots (*1*). There the invading tubercle bacillus is phagocytosed by a polymorphonuclear leukocyte, and is transported to a regional lymph node. Poisoned by its engulfed prey, the leukocyte disintegrates, mononuclear cells appear, and tubercle formation begins. The process may remain localized and healing by calcification may occur; or, there may be local spread by direct extension through the lymph node capsule; or, bacilli may be transported via lymphatics to other regional lymph nodes; or, they may find their way into the blood stream and become widely and rapidly disseminated (*3*).

The pathologic changes in the local scrofulous process are divided by Bailey (*1*) into four stages. In stage 1, there is a caseation within the lymph node; in stage 2, disruption of the lymph node capsule with periadenitis; in stage 3, rupture through the deep cervical or other fascia, with collar button abscess; and in stage 4, perforation of the abscess through the skin with open drainage.

Clinically, the patient first notes swelling in the area of one or more groups of lymph nodes. The onset is seldom acute, and discomfort rather than pain is noted. There may or may not be history of previous similar episodes or of other tuberculous manifestations. Physical examination reveals regional or general lymphadenopathy, with cold abscess or sinus formation, depending on the pathologic stage of the process at the time of examination; there may be slight fever and evidence of coincident tuberculosis; and a complicating disease may be present. In support of the physical findings are a positive tuberculin test, a normal leukocyte count with relative lymphocytosis, and an elevated erythrocyte sedimentation rate. Anemia may be present in debilitated persons. Roentgenograms may reveal old lymph node calcifications in the neck or in other localities. Despite the most careful evaluation of the evidence, biopsy may be necessary to eliminate other lymphadenopathies, such as Hodgkin's disease. Boeck's sarcoid, and lymphopathia venereum. A serological test should be routinely done to rule out the bubo of syphilis.

There are five methods currently employed, alone or in combination, in the treatment of scrofula. These are: rest, heliotherapy, high voltage roentgen therapy, surgery, and streptomycin. Of these, rest, heliotherapy, and roentgen therapy are supportive measures, stimulating the local or general resistance of the body to the tubercle bacillus. Surgery is intended to remove the infected tissue. Streptomycin alone acts directly on the tubercle bacillus, interfering with its normal pathogenic activities (*4*). One would expect that a measure aimed against the invader would be, if not an exterminative, an incomplete treatment; in fact, such has proved to be the case.

In 1946, Hinshaw, Feldman, and Pfuetze (*5*) reported fistula closure in 2 of 5 cases of tuberculous lymphadenitis with sinus formation treated with streptomycin. In 1947 the Council on Pharmacy and Chemistry (*6*) found variable results in "a number" of noncaseating cases. Feldman and Hinshaw (*4*) reported success in "a high percentage" of cases (total number unstated) where sinus existed. Shameskin et al. (*7*) had success in 1 of 2 cases without sinus. Flory and others (*8*) reviewing the results of streptomycin treatment from the point of view of pathologic changes in tissue, found evidence of success in 2 out of 5 cases, none with sinus. Lester (*2*) using the drug as an adjunct to surgery, reported success in 10 out of 11 patients. Most recently, the Council on Pharmacy and Chemistry (*9*) found that in 51 patients with draining sinus, 45 improved; and in 36 without sinus, 12 were cured and 18 improved. They concluded that "lymphadenitis responded reasonably well to treatment with streptomycin."

In this hospital we have had opportunity to observe the effects of streptomycin in the treatment of 7 patients with scrofula in the past 18 months. This number of cases is small, but it represents 4.3 percent of the 163 cases of tuberculosis of all forms diagnosed during that period. Also, in a disease now considered rare, it constitutes a considerable number. All the patients were hospitalized and were kept either at bed rest or confined to the ward during treatment. One patient was initially treated elsewhere and came to us in relapse. This man had also received high voltage roentgen therapy. Otherwise, streptomycin and rest were the only therapeutic measures employed. The diagnosis in all cases was established by biopsy. Except where specified, roentgenograms of the chest were negative.

CASE REPORTS

Case 1.—E. F. E., a 24-year-old Filipino, was admitted to the U. S. Naval Hospital, Portsmouth, Va., on 23 September 1947, complaining of a swelling over his right jaw of 3 weeks' duration. Treatment with sulfadiazine and penicillin elsewhere had been ineffective. Physical examination showed enlarged right preauricular and anterior cervical lymph nodes. A tuberculin test (using purified protein derivative, first strength) was strongly positive. Biopsy showed "necrotic lymphoid tissue." He was placed at bed rest and given streptomycin, 1.0 gm. daily to a total dose of 61.5 gm. Several months were allowed for convalescence. He was discharged on 23 July 1948, at which time the nodes were small and hard. On 18 November 1948 he was readmitted because of submental lymphadenitis. Biopsy revealed "a large area of central caseation" in a tuberculous lymph node.

Comment.—This case was in an early pathologic stage when treated with streptomycin. The most likely portal of entry was the ocular conjunctiva. The disease appeared to be favorably influenced by streptomycin, but the effect was short-lived, and lymphatic extension to another area soon occurred. The treatment with streptomycin must therefore be regarded as a failure.

Case 2.—F. G., a 22-year-old white man, was admitted 23 August 1948. He gave a history of drinking raw milk on the farm in childhood. At the age of 10 years, he had swelling in his neck on both sides which "stuck out as far as my ears." These were incised by a physician, and drained pus for several months. He was well until his twenty-first year when, in November 1947, he noted painful lumps in the left side of the neck. He was admitted to another naval hospital, where examination showed a "large swelling" below the left ear, external to the sternocleidomastoid muscle. A roentgenogram of the neck showed old lymph node calcifications. Biopsy showed "acute adenitis" in one node, and "caseous center, fibrous outer edge, minimum lymphoid tissue with heavy calcification" in another, "most probably tuberculous in origin." The tubercle bacillus was demonstrated on smear. He was treated with rest, streptomycin (90 gm. in 90 days), and simultaneous high voltage roentgen therapy (total 732 R units). He was readmitted to this hospital because of local recurrence of glandular swelling. Examination showed a robust young man with slight left anterior cervical lymphadenopathy and threatened sinus formation. There were old surgical scars present in the neck bilaterally. He was treated with bed rest followed by gradual exercise over a period of 6 months. Under symptomatic treatment the lymph nodes became small and hard. By February 1949 return to full active duty was possible.

Comment.—This case illustrates the chronicity of scrofula and the ability of the tubercle bacillus to lie dormant in lymph nodes for 11 years. It also illustrates the ability of a vigorous youth to combat the disease, (on two occasions) with minimal treatment. Pathologically, it was in stage 3 when first seen here. It must be considered that both streptomycin and high voltage roentgen therapy failed in this case.

Case 3.—J. A. J., a 23-year-old Negress, was admitted to the hospital on 16 April 1948. In 1940, at the age of 15, she was found to have pulmonary tuberculosis, and was treated with right pneumothorax. In 1944 the disease was considered to be arrested, and the lung was allowed to reexpand. At the age of 22, in April 1947, she first noted a transient swelling in her neck. This recurred in November 1947, and progressed in size until her admission. Physical examination at that time showed definite enlargement of the cervical lymph nodes in the right anterior and posterior cervical triangles, and a lesser enlargement of the lymph nodes in the left side of the neck. Biopsy was reported to show tuberculous lymphadenitis. Roentgenograms showed no evidence of previous lymphadenitis or of active pulmonary disease. The erythrocyte sedimentation rate was 24. She received streptomycin, 1.0 gm. daily, for 42 days. There was little immediate response, but 4 months after the termination of treatment, when last seen, the glands were smaller and more firm and the patient was subjectively well.

Comment.—This is a case with a pulmonary portal of entry, lymphatic spread to the regional mediastinal lympth nodes, and, after a 7-year period of dormancy, further lymphatic spread to the cervical lymph nodes. Pathologically, it was in stage 2. Streptomycin was probably beneficial, although the ultimate prognosis remains unknown. There is not too much reason for gratification, since she had already experienced a spontaneous remission of the lymphadenitis about 1 year prior to the use of the drug.

Case 4.—H. A. Y., a 24-year-old white man, was admitted 19 April 1948 complaining of abdominal pain, bloating, and belching of about 1 week's duration. There was a past history of treatment for "mesenteric lymphadenitis" at the age of 9. Physical examination revealed a temperature of 99.6° F., a tender mass about

2 cm. in diameter in the left lower quadrant of the abdomen, and moderate abdominal distention. A tuberculin test was strongly positive. The erythrocyte sedimentation rate was 22. Roentgenograms of the abdomen disclosed a large calcified mass in the mesentery opposite the fifth lumbar vertebra. A diagnosis of tuberculous mesenteric lymphadenitis was made. Because of threatened intestinal obstruction, treatment with a Miller-Abbot tube was necessary, also treatment with streptomycin, 1.0 gm. daily, was begun. Within 1 week the patient was symptom-free and his fever had disappeared. Later the gastrointestinal tract was examined roentgenographically with a barium meal. This showed partial small bowel obstruction. Streptomycin was continued to a total dose of 40.0 gm. The abdominal mass shrank, but did not disappear. On discharge, 12 August 1948, the patient was clinically well.

Comment.—This case is an example of an intestinal portal of entry, long dormancy, and local recurrence. In all probability, the local periglandular tissues (mesentery and intestinal wall) were involved. Streptomycin apparently obviated surgical intervention for intestinal obstruction, which, in the circumstances, might well have resulted in chronic fistula formation. Even if there is recurrence later, the drug served its purpose at the time.

Case 5.—L. R., a 24-year-old Negro, was admitted on 27 March 1948. He complained of the loss of 60 pounds of weight in the past 8 months, accompanied by nervousness and sweats. In the 10 days prior to admission he had had fever, chills, swelling of the ankles, and painful lumps in the groin. Physical examination showed an acutely ill man with a temperature of 102° F., pulse 120, and blood pressure 145/70. There was emaciation, exophthalmos, diffuse goiter, swollen legs, tender ankles, and generalized lymphadenopathy. The inguinal lymph nodes were tender. There was slight anemia. The Frei intradermal reaction was positive. A therapeutic test for lymphopathia venereum with sulfadiazine was unsuccessful. Lymph node biopsy showed tuberculosis. The basal metabolism rate, taken in a fever-free interval, was plus 51 percent. A diagnosis of simultaneous hyperthyroidism and tuberculous lymphadenitis was established. Streptomycin, 1.0 gm. per day, and propylthiouracil were administered. The total dose of streptomycin was 42.0 gm. The patient regained 30 pounds of weight, and the lymph nodes became smaller and harder. On 4 August 1948 a subtotal thyroidectomy was performed. (Pathologic diagnosis: "Hypertrophic parenchymatous coloid thyroid.") On 15 August 1948 the basal metabolism rate was minus 15 percent. On discharge, 20 August 1948, he was subjectively and objectively well.

Comment.—In this case of simultaneous hyperthyroidism and tuberculosis of the lymph nodes, the portal of entry of the tubercle bacillus is unknown. Pathologically, the lymphadenitis was in stage 1. Streptomycin was probably life-saving, since without it, subtotal thyroidectomy would probably have been followed by complications. This is another instance in which, even if there be relapse, the drug was of great value at the time it was used.

Case 6.—J. G., a 23-year-old Negro, was admitted to the hospital on 13 October 1948 complaining of lumps in the groin. A "cyst" had been incised in the right groin 4 months previously, with evacuation of pus. Lymph node biopsy showed "hyperplastic, noncaseating tuberculosis." Physical examination showed low grade pyrexia and generalized lymph node enlargement, especially noticeable in the inguinal areas. A roentgenogram of the chest showed extremely enlarged hilar lymph nodes. The second strength purified protein derivative gave a positive reaction. Apart from this and except for the evidence on biopsy, the clinical picture suggested Boeck's sarcoid. Forty-two grams of streptomycin

were administered in 42 days. There was some regression of the surface, but none of the hilar lymph nodes. No follow-up is available.

Comment.—The portal of entry in this case is unknown. Spread was probably miliary. Pathologically, the process was in the first stage. The observed effects of streptomycin were minimal.

Case 7.—E. B., a 23-year-old white man, was admitted to the hospital on 19 November 1948. As a child, he drank raw milk on the farm. He stated that the herd was tuberculin tested. In July 1948 he noted a lump in the right armpit. On admission, enlarged right axillary lymph nodes were found. On aspiration, pus was encountered. Biopsy showed tuberculous lymphadenitis. A fistula developed at the site where tissue was removed for biopsy. He received 47.0 gm. of streptomycin in as many days. The fistula closed in about 1 month. On 8 April 1949 lymph nodes were normal in size.

Comment.—The portal of entry in this case is unknown. The disease progressed rapidly, partly as a result of diagnostic procedures, from pathologic stage 2 to stage 4. Streptomycin apparently arrested the disease, but the follow-up is too short to justify the word "cure."

COMMENT

The results from the use of streptomycin in these seven cases of tuberculous lymphadenitis may be summarized as follows: The immediate treatment result was poor in one, and good in six. In two, the drug was unquestionably of great value, regardless of the eventual outcome, since in one it obviated surgery for intestinal obstruction, and in the other it prepared the patient for operation for coincident thyrotoxicosis. On the other hand, in two, in whom a follow-up of 1 year was possible, relapse occurred. This fact renders enthusiasm based on an initial success unwise.

In the two who showed relapse, the recurrent lymphadenopathy subsided over a period of months under treatment with rest and heliotherapy. Since recovery was not uncommon in the prestreptomycin era with these simple measures, there is reason to doubt the desirability of using this drug in the ordinary case of scrofula, the more so since the tubercle bacillus is likely to become resistant to streptomycin, and it may later be ineffective when more urgently needed by the patient.

It will be noted that most of our patients were in an early stage and that fistula formation occurred in only one. This patient responded promptly to the drug. This is in accord with the usual observation that streptomycin is most useful in so-called surgical tuberculosis where drainage exists.

In general, it is probable that streptomycin alone is not a complete treatment for tuberculous lymphadenitis and that it is best reserved for use in the case with fistula or other complication.

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A PRELIMINARY REPORT ON HYDROCEPHALUS, SPINA BIFIDA AND OTHER CONGENITAL ANOMALIES IN THE RAT PRODUCED BY TRYPAN BLUE, by J. Gillman; Christie Gilbert; T. Gillman; and Isobel Spense. The South African Journal of Medical Science 13: 47–90, March 1948.

Gillman et al. injected trypan blue into rats. Gross malformations such as ocular defects, spina bifida, tail defects, and hydrocephalus appeared in 19.2 percent of the offspring. If the female rat received an injection before conception as well as an additional dose during pregnancy, 25 percent of the offspring were abnormal. By giving an injection of trypan blue on the seventh day before conception and the seventh day after conception, 80 percent of the litter were abnormal; if only one injection was given on the day before conception 25 percent of the litter were abnormal. A high neonatal mortality, a reduction in the size of the litter, a low birth rate, and a retardation of postnatal development was manifest. They found that trypan blue was bound to the plasma albumin and did not enter the fetus or the amniotic fluid or amniotic epithelium, and that all embryonic tissues except the yolk sac were free. They believe that trypan blue causes anomalies in an offspring by producing such preceding metabolic disturbances as to interfere with the subsequent fetal development.—*Abstract.*

About the Army Medical Department

III. Emergency Personnel Planning [1]

PAUL I. ROBINSON, *Colonel, MC, U. S. A.*[2]

A LETTER to the surgeons of major overseas commands concerning the anticipated shortage of medical officers that will occur this summer was quoted in the March issue of the Armed Forces Medical Journal in order that the various steps in planning to meet this particular emergency could be seen.

A few days after this letter was dispatched a meeting was held with the Deputy Chief of Staff, U. S. Army, in which all phases of the problem were discussed. Not the least among the problems to be surmounted in sending a large number of physicians overseas for 3 months were the funds from which their temporary duty travel and per diem could be paid. The Surgeon General was willing to curtail much of the ordinary temporary duty travel of his own personnel in order to meet the emergency. It was considered unfair to prevent officers so assigned from receiving the normal per diem. It was, therefore, decided that per diem would be furnished in accordance with the present regulations, which are determined in each case but in general might be said to be as follows: (*a*) $7 a day for the first 30 days, if no quarters are available; (*b*) $4 a day if quarters are available; (*c*) $4 a day for the second 30 days, if no quarters are available; (*d*) $2 a day if quarters are available; (*e*) $2 for any period after the second month, if no quarters are available; and (*f*) no per diem if quarters are available.

The personnel staff officers of all major overseas commands were in Washington at the time of this meeting and the proposition was presented to them, with the inquiry as to whether transportation within the command would be charged against these temporary duty

[1] Continued from the March issue.
[2] Personnel Division, Office of the Surgeon General.

funds. It was universally stated that travel within the command would be by Government transportation. The personnel representatives also stated that bachelor officers' quarters would be furnished to every officer. These two facts lowered the amount of temporary duty funds required to the point that they could be met by the Department of the Army. The officers from the various commands were asked if careful planning could be accomplished within the command to assure no waste of time, in order that each officer sent on temporary duty could be used to the fullest extent. All stated that this planning would be accomplished.

Thus, it was determined that no more than 100 residents would be used on this temporary duty. The Navy was unable to loan the Army any physicians who were on active duty but was willing to ask for Reserve medical officers to come on duty for this period if the Army so desired. The Army also considered whether or not it was feasible to ask Reserve medical officers to come on duty for this period. It was determined that only sufficient funds were available to send the 100 residents previously mentioned. In view of the emergency nature of this problem and the administrative difficulties involved in ordering Reserve officers to active duty, it was not considered practicable to use such personnel. It was further decided that the number of medical officers on duty in the Army areas could not be reduced, even temporarily, without endangering military preparedness. The use of civilian physicians in overseas commands was not practicable because their allowances would have to come from funds which are extremely limited.

The next step was to send a letter to the hospitals with their quotas by military occupational specialty number. The situation was carefully explained so that everyone in the teaching hospitals would be thoroughly cognizant of the nature of the emergency. Each of the hospitals was asked to supply the Personnel Division of the Surgeon General's Office with the names of the officers selected to fill the various quotas. The same proportion of residents was taken from each of the hospitals—with due allowance for programs in which there was only one resident. Each hospital was notified that the selected officers would be authorized per diem and that air transportation would be furnished from the United States to the command. They were also told that dependents could not accompany the officers for this period of duty. Only first- and second-year residents were selected because it was to everyone's advantage to allow the senior residents to finish their program and thus become available for regular duty on 1 July. Everyone was notified that those used in this emergency would go back into the training program for the completion of their

current year of training, even though it extended their time in the hospitals.

This program was received with reasonable enthusiasm by the residents themselves. In only a few instances was it necessary for the hospital commanders to make the selection since the quota was largely filled by volunteers. This plan has the advantage of allowing these residents to visit remote places for a short time, in addition to rendering a distinct service to their country.

The overseas commands, while not satisfied with the number of medical officers being furnished indicated that they were satisfied with the efforts we were making to assist them in this period. Much of the elective medical and surgical work that would ordinarily be done during these months will have to be curtailed.

Since the Air Force also has residents in the Army teaching hospitals, the Surgeon General of the Air Force was advised of our plan and the policy was established that should any of the officers selected to fill this quota transfer to the Air Force, orders would be issued for these officers to complete the emergency mission.

The surgeon of one of the overseas commands stated that he would like it explained to all officers that the bachelor quarters available are not luxurious; and opportunities for travel on pass or leave will be almost impossible during the period when the officers are on temporary duty. He strongly urged that wives do not visit their husbands while they are overseas because hotel or other living accommodations could not be provided for them and their expenses would be high. Aside from these considerations everything will be done to make the tour of temporary duty both pleasant and profitable.

In addition to these emergency measures concurrent planning for permanent assignments is proceeding normally. About 260 medical officers on Reserve status have been sent a questionnaire in which they were asked to state their preference for assignments, their present family situation, and other pertinent information that would be useful in determining their assignment. Fourteen have already indicated their preference for a Regular Army career and have applied for a Regular Army commission. Selections will be made from this group for a few openings in the newly established courses in military medicine to be given this fall and winter at the Army Medical Center, Washington, D. C., and the Army Medical Center, Fort Sam Houston, Tex.

The overseas commands have preference on the remainder of the available officers. The combined requirements for officers having the qualifications of this group are 241. The number available falls short of the goal by 18 percent. A numerical goal, by command, was therefore established to fill 82 percent of the requirements for each of the

overseas commands. Requirements for the Far East Command can never be met from first choices; whereas, the opposite is true of the European Command. Because there are many locations in the Far East Command where living conditions are not suited to family life, single officers were placed on the Far East list. There were still 23 officers to be selected and this selection was made from married officers who did not have children and from officers who contemplated marriage before the date of their shipment.

Selections of a few officers had to be made for the smaller commands such as Trieste and Alaska. To meet the quota for Trieste, a single officer was selected who had made a special plea for assignment to the European Command because of the Holy Year, since he was a Catholic. Further justification for the selection of a single officer for this assignment was a recent directive regarding nonshipment of dependents to Trieste because of the generally poor housing accommodations. The quota for Alaska was two officers. After carefully screening those available one officer from northern Wisconsin and one from North Dakota were selected; one was married and had no children; the other was single. These two officers were selected because of the probability that they would enjoy an assignment in a cold climate better than officers who had not been accustomed to Northern climates.

The list was then reviewed for officers to fill the quota of 16 for the Caribbean Command. Quarters are generally available for married personnel in the Caribbean Command and only married officers with dependents were selected for this assignment. Another criterion that was used was nearness to the port of embarkation in order that the maximum amount of travel funds could be conserved. Of the remaining group, two officers had indicated a preference for Hawaii. These two were selected to meet the quota of 16, the rest being selected from married officers who had named the Caribbean Command as first or second choice, but were closer to San Francisco than to the east coast. The Caribbean Command is very popular with any group that is asked to submit its preferences, because of its nearness to the United States and the generally good living conditions.

These selections left a group who had all given the European Command as first choice. All were married, although not all of them had children. To meet a quota of 5 for Austria, 4 were selected alphabetically from the top of the list. One single officer was selected for assignment to Austria because of his ability to speak Czechoslovak. Nine officers from this group have indicated that they expect to have children born this summer. All of them have been temporarily assigned as near to their homes as possible, and their shipment to overseas stations has been deferred until after 1 January 1951. These are

a few examples of our attempts to individualize assignments insofar as possible. The Personnel Division is striving to improve its career assignments as they pertain to the use of personnel, and is always glad to discuss with any officer the reasoning that has gone into his particular assignment.

CAUSES FOR AMPUTATIONS PERFORMED AT WALTER REED GENERAL HOSPITAL DURING 1947 AND 1948, by August W. Spittler, *Colonel, MC, U. S. A.;* and Lloyd W. Taylor, *Lieutenant Colonel, MC, U. S. A.* Journal of Bone and Joint Surgery **31A**: 800–804, Oct. 1949.

Although no amputations were performed for osteomyelitis alone, this disease still takes first place as a major contributing cause of amputation. Except for apparent systemic benefit to a patient during acute flare-ups of osteomyelitis, sulfonamides and antibiotics have contributed little to the cure of adult patients with chronic draining osteomyelitis. In planning a reconstructive program of rehabilitation on an injured extremity, the percent of successful end results is in inverse ratio to the number of operations required to produce that result.

The authors conclude that: (*a*) Unilateral amputation is not a contra-indication to amputation of the contralateral extremity; (*b*) skin grafting of any type to full weight-bearing surfaces is so highly unsatisfactory as to condemn the procedure; (*c*) elective sacrifice of the fibula in a reconstructive program is highly unsatisfactory; (*d*) a Syme's amputation is the best major amputation through an extremity; (*e*) when amputation is a possibility, surgical incisions should be placed in such a manner as to insure amputation at the lowest possible level should this procedure later become necessary; (*f*) when amputation is a possibility, the removal of cancellous graft from the ilium should be accomplished on the affected and not on the contralateral side; and (*g*) needless operative procedures that promised little possibility of success were performed on many of the patients studied, causing prolonged months of hospitalization, psychic trauma, and generalized systemic damage, secondary to prolonged periods of chronic infection. Early evaluation of these cases, and applying sound surgical principles could have prevented many of these undesirable results. The principle most often disregarded in these cases was that amputation is a sound method of treatment and not a last resort.—*Abstract.*

THE PHYSICIAN MUST KNOW WHAT HIS PREDECESSORS HAVE KNOWN IF HE DOES NOT WISH TO DECEIVE BOTH HIMSELF AND OTHERS.—*Hippocrates.*

EDITORIAL

The Periodic Physical Examination

The primary function of the physician is to recognize disease in its earliest phase in the asymptomatic person. This must be a fundamental concept in the practice of medicine if the physician is to avoid the dilemma of recognizing a disease when its symptoms and signs are pathognomonic and evidence of advanced pathologic changes—it is then too late for early and effective treatment.

Except in the fulminating types of organic diseases and the acute infections, a period of a year or two exists between the time of the appearance of early pathologic tissue changes and pathognomonic signs and symptoms. It is in this interval, and particularly during the early phases of the pathologic process, when the diagnosis must be made. The symptoms then are apt to be vague and of a minor nature, and thus may be misleading, or the patient may be asymptomatic. However, upon examination, clinical and laboratory evidence of disease can often be detected.

Examples of this period of latency are the following: (*a*) When malignant tissue remains after surgical resection, the interval between surgical removal of the cancer and the recurrence is about 15 to 20 months, or longer. If this is the latency period when cancer is already present, then the interval between the time of earliest tissue invasion and the time of appearance of the textbook description of a chronic organic disease or a malignant lesion probably is much longer. In the interval the patient may have been asymptomatic or else symptoms of a vague or minor nature may have been present. (*b*) The normal kidney can excrete urine of a specific gravity of 1022 or higher; if the kidney cannot excrete urine of a specific gravity higher than 1020 there exists moderate glomerular and tubular injury. When the kidney cannot excrete urine of specific gravity over 1010 it has undergone extensive glomerular and tubular damage, and extensive fibrosis. During this period of progressive pathologic changes, the patient probably remained asymptomatic until the symptoms of glomerulonephritis, such as dependent edema, dyspnea, and headache, appeared.

(*c*) In arteriolar nephrosclerosis, mild renal damage may exist and yet there may be no alteration in the chemistry of the urine because the minimal increase in blood pressure was sufficient to supply the glomeruli and the tubules with the necessary amount of blood under adequate pressure and, therefore, glomerular filtration remained normal. When albuminuria, cylindruria, hypertension, and edema appear the pathologic renal changes are then already far advanced. (*d*) Sir Thomas Lewis observed that if the total capacity of the healthy heart for work is taken at 10 units, only one unit is required to maintain a normal circulation while the body is at rest; the remaining 9 form the reserve. He points out that, in cardiac failure, by the time congestion sets in, nine-tenths of the heart's capacity to perform its task have been lost. In this interval the only symptoms indicative of cardiac disease may have been breathlessness occurring after some act previously performed without undue breathlessness, or the occurrence of vague precordial discomfort or palpitation.

There are many chronic diseases in which the detection of an organic or neoplastic lesion in an asymptomatic person lies within the capabilities of the physician, provided periodic physical examinations are done and provided clinical acumen is correlated with every means of diagnosis ordinarily available. To do this requires (*a*) an evaluation of a thorough, detailed, clinical history paying particular attention to vague or what appear to be minor complaints. Often a careful interrogation will be required to elicit symptoms which the patient may not otherwise volunteer. (*b*) The examiner must seek evidence of the presence of organic changes rather than physical defects which reflect changes in function incident to age and which do not affect health. The thorough physical examination, in addition to percussion, auscultation, and palpation, must include an inspection of every visible organ and tissue—the larynx, as well as the cervix, rectum, and the sigmoid; palpation of the breast, digital examination of the rectum in the knee-chest position (4 out of 5 rectal carcinomas are within the reach of the examining finger), and of the prostrate always must be done; and a sigmoidoscopic examination is necessary to detect malignant changes anywhere below the middle third of the sigmoid.

To imply that a negative result obtained after percussion and auscultation of the lungs of the asymptomatic person is indicative of the absence of organic or neoplastic lesion of the lung, jeopardizes the physical welfare of the person examined. A roentgenogram of the lungs must be made on a 14×17-inch film if a peripheral organic or neoplastic lung lesion is to be discovered at the earliest possible moment. A roentgenologic study of the stomach and the gastrointestinal tract must be done whenever there is a family history of gastric carcinoma. A hemoglobin determination and red and white blood cell

counts are required to detect disease of the hemopoietic system; and the entire quantity of urine excreted during a period of 24 hours must be examined, for it is not possible to estimate the function of all the glomeruli and the tubules if only a single specimen of urine is examined. An electrocardiogram and other clinical and laboratory examinations including the method of cytologic diagnosis of Papanicolaou, will be required, depending upon the evaluation of clinical history and physical findings.

If a disease is to be arrested or cured early, the diagnosis must be made in the interval between the occurrence of the early pathologic tissue changes and the appearance of pathognomonic signs and symptoms. This is the challenge that the physician must meet if progress in the methods of clinical diagnosis is to keep pace with the recent advances in biochemistry, surgical technique, and therapeutics.

—J. L. S.

BOOK REVIEWS AND BOOKS RECEIVED

Publishers submitting books for review are requested to address them as follows:

The Editor,
UNITED STATES ARMED FORCES MEDICAL JOURNAL,
Bureau of Medicine and Surgery, Navy Department,
Washington 25, D. C.

(For review)

OPERATIVE TECHNIC IN SPECIALTY SURGERY, edited by Warren H. Cole, M. D., F. A. C. S., *Professor and Head of the Department of Surgery, University of Illinois College of Medicine; Director of Surgical Service, Illinois Research and Educational Hospitals, Chicago.* Introduction by Allen O. Whipple, M. D., F. A. C. S. 725 pages, illustrated. Appleton-Century-Crofts, Inc., New York, N. Y., publishers, 1949. Price $14.

This book is made up of a composite group of chapters, each devoted to a different branch of surgery. Each is written by a different author who is well-known as an outstanding authority in his field. The book contains much information of interest to the student and specialist but will be of most interest to the general surgeon whose work is more or less involved with most of the surgical specialties. There are no chapters dealing with ophthalmology or otolaryngology. The book is not an atlas nor is it a reference library, but it is a useful adjunct to a surgeon's library as it contains much condensed practical and up-to-date information on operative therapeutics.

The opening chapter deals with plastic surgery in which the general principles are stressed more than specific details of individual operations. However, some of the procedures are illustrated by multiple-stage illustrations. Following this is a chapter on thoracic surgery and repair of diaphragmatic hernias. The operative procedures for various thoracic lesions are described except for the heart, which, together with the mediastinum, is covered in the chapter that follows. The latter is particularly interesting in its description of how to repair penetrating wounds of the heart and how to recognize cardiac compression. Following this there are several chapters devoted to orthopedic surgery beginning with the operative therapy of fractures, then one about osteomyelitis, followed by one on deformities and neoplasms of bone, proceeding to a chapter which deals with operative approaches to joints and containing some excellent illustrations, followed by a final chapter which discusses the surgical procedures used to help correct the deformities caused by spastic paralysis and anterior poliomyelitis.

The next five chapters deal with surgery in relation to the various parts of the nervous system and its coverings. The first of these involves the general principles of closure of scalp wounds, the method for preparing a flap in different areas of the scalp and closure of defects, and finally the method of dealing with various brain lesions. Next is a chapter devoted to the surgical problems which

can be performed on them. A chapter dealing with the peripheral nerves contains a number of good illustrations showing the proper approaches, and the disfiguring scars resulting from poorly planned approaches. The materials used in repair and the technique of suturing nerve trunks are discussed and illustrated. The last chapter on the nervous system concerns the various types of sympathectomy together with the technique of performing these operations as well as the method used to perform a lumbar and thoracic paravertebral sympathetic block.

In a chapter on gynecological surgery the author describes a method for performing all the usual types of pelvic surgery and gives the indications, together with the advantages and disadvantages to be considered. A more lengthy discussion of the procedure used in radical hysterectomy for cervical cancer, and that for radical groin dissection in cancer, is included.

The final chapter is devoted to the male genito-urinary system and following a short opening discussion of anatomical considerations, symptoms, and methods of diagnosis, the author discusses the operations performed in that region.

In conclusion it may be stated that this is an up-to-date treatise written by a group of America's leading surgical specialists. The discussions are short and to the point, and written so that the directions are readily followed. A bibliography is included at the end of each chapter. It is an excellent book for the practicing surgeon who wishes to learn what an excellent authority does without searching through lengthy volumes.—*Commander C. D. Burroughs, (MC) U. S. N.*

ORGANIC CHEMISTRY IN PHARMACY, edited by Charles O. Wilson, Ph. D., *Professor of Pharmaceutical Chemistry, Chairman of the Department of Pharmaceutical Chemistry, College of Pharmacy, University of Texas;* and Ole Gisvold, Ph. D., *Professor of Pharmaceutical Chemistry, Chairman of the Department of Pharmaceutical Chemistry, College of Pharmacy, University of Minnesota.* 8 authors. 622 pages; illustrated. J. B. Lippincott Co., Philadelphia, Pa., publishers, 1949. Price $9.

With the assistance of a staff of experts, the authors have produced an up-to-the-minute text that should be welcomed by teachers, students, and professional pharmacists.

The book has as its stated objective the presentation of the essential pharmaceutical knowledge of the organic chemical substances used in pharmacy and medicine. As a text, it is designed for a course in organic pharmaceutical chemistry based upon a general course in organic chemistry and preceding courses in pharmacology. To fit into this position in the curriculum, each chapter is opened with a review of the basic principles of the class, and to orient the student in the relationship between chemical structure and pharmacological uses, chapters are included on physical properties in relation to biologic action and metabolic changes of drugs and related organic compounds in the body. In addition, brief references are made to pharmacologic action in the discussion of individual compounds.

Compounds are presented in the order of chemical constitution as aliphatic, aromatic, heterocyclic, and other cyclic types, with special chapters on sulfur compounds, compounds containing heavy metals, dyes, surface-active agents, alkaloids, antibiotics, vitamins and proteins, and amino acids. Working formulas are given where feasible and all important structural formulas have been incorporated in the text. In areas of active research, the authors look forward with the inclusion of many compounds which are still in the laboratory stage of development.

In striking contrast to most organic chemistry books, this one is scientifically accurate and at the same time is pleasantly readable. It is well indexed, and

many original source references are given. It is well arranged and excellently printed. Organic Chemistry in Pharmacy will be well received and will be a valued addition to the literature of pharmacy.—*Commander W. P. Briggs, (MSC) U. S. N.*

BOOKS RECEIVED

Receipt of the following books is acknowledged. As far as practicable, these will be reviewed at a later date.

NEUROLOGY, by Roy R. Grinker, M. D., *Director of the Institute for Psychosomatic and Psychiatric Research and Training and Chairman, The Department of Neuropsychiatry of the Michael Reese Hospital, Chicago, Ill.*; and Paul C. Bucy, M. D., *Professor of Neurology and Neurological Surgery, University of Illinois College of Medicine, Chicago, Ill.* 4th edition, completely revised and reset in new type. 1,138 pages, illustrated. Charles C Thomas, Springfield, Ill., publishers, 1949. Price $12.50.

THE PRACTICE OF REFRACTION, by Sir Stewart Duke-Elder, K. C. V. O., M. A., D. Sc. (St. And.), Ph. D. (Lond.), M. D., F. R. C. S., Hon. D. S. C. (North Western), *Surgeon-Oculist to H. M. The King; Knight of Grace of the Order of St. John; Consulting Ophthalmic Surgeon to the Army and the Royal Air Force; Director of Research, Institute of Ophthalmology, University of London; Consulting Ophthalmic Surgeon, Moorfields Westminister and Central Eye Hospital; Ophthalmic Surgeon, St. George's Hospital.* 5th edition. 317 pages; with 216 illustrations. The C. V. Mosby Co., St. Louis, Mo., publishers, 1949. Price $6.25.

HUMAN HELMINTHOLOGY, A Manual for Physicians, Sanitarians, and Medical Zoologists, by Ernest Carroll Faust, A. B., M. A., Ph. D., *The William Vincent Professor of Tropical Diseases and Hygiene, Head of the Division of Parasitology, Department of Tropical Medicine and Public Health, The Tulane University of Louisiana, New Orleans, La.* 3d edition, revised. 744 pages, illustrated. Lea & Febiger, Philadelphia, Pa., publishers, 1949. Price $10.

ROENTGEN DIAGNOSIS OF THE EXTREMITIES AND SPINE (Annals of Roentgenology, Vol. XVII), by Albert B. Ferguson, M. D. 2d edition, revised and enlarged. 519 pages, illustrated. Paul B. Hoeber, Inc., New York, N. Y., publishers, 1949. Price $15.

HEMATOLOGY FOR STUDENTS AND PRACTITIONERS, by Willis M. Fowler, M. D., *Professor of Internal Medicine, University of Iowa, Iowa City, Ia.*, with a chapter by Elmer L. DeGowin, M. D., *Associate Professor of Internal Medicine, University of Iowa, Iowa City, Ia.* 2d edition, revised. 535 pages, illustrated. Paul B. Hoeber, Inc., New York, N. Y., publishers, 1949. Price $8.50.

MALIGNANT DISEASE AND ITS TREATMENT BY RADIUM, by Sir Stanford Cade, K. B. E., C. B., F. R. C. S., M. R. C. P., *Surgeon, Westminister Hospital, Mount Vernon Hospital and Radium Institute; Lecturer in Surgery, Westminister Hospital Medical School and formerly Examiner in Surgery, University of London; Member of the Court of Examiners, late Hunterian Professor and Arris and Gale Lecturer; Royal College of Surgeons of England; Member of the National Radium Commission and Trust; Consultant in Surgery to the Royal Air Force,* with a Foreword by Sir Ernest Rock Carling, F. R. C. P., F. R. C. S., F. F. R., *Consulting Surgeon and Vice-President, Westminister Hospital.* Volume II, 2d edition. 430 pages, illustrated. The Williams & Wilkins Co., Baltimore, Md., publishers, 1949. Price $12.50.

TEXTBOOK OF MEDICINE, edited by Sir John Conybeare, K. B. E., M. C., D. M. (Oxon.), F. R. C. P., *Physician to Guy's Hospital, London.* 9th edition. 875 pages, illustrated. The Williams & Wilkins Co., Baltimore, Md., publishers, 1949. Price $8.

HELP YOURSELF TO BETTER SIGHT, by Margaret Darst Corbett. 218 pages. Prentice-Hall, Inc., New York, N. Y., publishers, 1949. Price $2.50.

OPERATIONS OF GENERAL SURGERY, by Thomas G. Orr, M. D., *Professor of Surgery, University of Kansas School of Medicine, Kansas City, Kans.* 2d edition. 890 pages with 1,700 step-by-step illustrations on 721 figures. W. B. Saunders Co., Philadelphia, Pa., publishers, 1949. Price $13.50.

MANUAL OF MEDICAL EMERGENCIES, by Stuart C. Cullen, M. D., *Professor of Surgery; Chairman, Division of Anesthesiology, State University of Iowa College of Medicine,* and E. G. Gross, M. D., *Professor and Head of Department of Pharmacology, State University of Iowa College of Medicine.* 267 pages, illustrated. Year Book Publishers, Inc., Chicago, Ill., publishers, 1949. Price $3.75.

FEMALE SEX ENDOCRINOLOGY, Concise Therapy, by Charles H. Birnberg, M. D., *Associate Obstetrician, Chief of Female Sex Endocrinology, and Endocrine Laboratory, Jewish Hospital of Brooklyn.* 134 pages, 30 illustrations including 3 in color. J. B. Lippincott Co., Philadelphia, Pa., publishers, 1949. Price $4.

KAYNE, PAGEL, AND O'SHAUGHNESSEY'S PULMONARY TUBERCULOSIS, Pathology, Diagnosis, Management and Prevention, revised and partly rewritten by Walter Pagel, M. D., *Pathologist, Central Middlesex County Hospital, London;* F. A. H. Simmonds, M. A., M. D., D. P. H., *Medical Director, Clare Hall County Hospital, Middlesex;* N. MacDonald, M. B., M. R. C. P., Ed., *Physician to the Chest Clinic, Redhill County Hospital, Middlesex;* L. Fatti, F. R. C. S., *Thoracic Surgeon, Hillingdon County Hospital and Harefield County Hospital, Middlesex.* 2d edition. 720 pages, illustrated. Geoffrey Cumberlege, Oxford University Press, New York, N. Y., publishers, 1948. Price $18.50.

EPILEPSY AND CONVULSIVE DISORDERS IN CHILDREN, by Edward M. Bridge, M. D., *Research Professor of Pediatrics, School of Medicine, University of Buffalo; Director of Research, Children's Hospital of Buffalo; Formerly Associate in Pediatrics, Johns Hopkins School of Medicine; and Physician in Charge, Johns Hopkins Epilepsy Clinic.* 670 pages, illustrated. McGraw-Hill Book Co., Inc., New York, N. Y., publishers, 1949. Price $8.50.

STOMACH DISEASE AS DIAGNOSED BY GASTROSCOPY, by Eddy D. Palmer, A. B., M. S., M. D., *Major, Medical Corps, United States Army. Formerly Chief, Gastrointestinal Section, Walter Reed General Hospital, Washington, D. C.* 200 pages; 53 black and white illustrations and 56 in color by Phyllis Anderson. Lea & Febiger, Philadelphia, Pa., publishers, 1949. Price $8.50.

DENTISTRY IN PUBLIC HEALTH, edited by Walter J. Pelton, B. S., D. D. S., M. S. P. H., *Dental Surgeon, U. S. Public Health Service, Colorado,* and Jacob M. Wisan, D. D. S., M. S. P. H., *Director, Joseph Samuels Dental Clinic, Rhode Island State Hospital, for the Dental Health Section of the American Public Health Association.* 363 pages; illustrated with 64 figures. The W. B. Saunders Co., Philadelphia, Pa., publishers, 1949. Price $5.50.

POLIOMYELITIS, Papers and Discussions Presented at the First International Poliomyelitis Conference, compiled and edited for the International Poliomyelitis Congress. 360 pages; illustrated. J. B. Lippincott Company, Philadelphia, Pa., publishers, 1949. Price $5.

1948 YEAR BOOK OF NEUROLOGY, PSYCHIATRY AND NEUROSURGERY. Neurology, edited by Hans H. Reese, M. D., *Professor of Neurology and Psychiatry, University of Wisconsin Medical School,* and Mabel G. Masten, M. D., *Associate Professor of Neuropsychiatry, University of Wisconsin Medical School.* Psychiatry, edited by Nolan D. C. Lewis, M. D., *Director, New York State Psychiatric Institute and Hospital; Professor of Psychiatry, Columbia University.* Neurosurgery, edited by Percival Bailey, M. D., *Professor of Neurology and Neurological Surgery, University of Illinois.* The Year Book Publishers, Inc., Chicago, Ill., publishers, 1949. Price $5.

OBESITY, by Edward H. Rynearson, M. D., F. A. C. P., *Division of Medicine, Mayo Clinic; Associate Professor of Medicine, Mayo Foundation;* and Clifford F. Gastineau, M. D., *Fellow in Medicine, Mayo Foundation, Rochester, Minn.* Edited by Willard O. Thompson, M. D., *Editor, Journal of Clinical Endocrinology; Clinical Professor of Medicine, University of Illinois College of Medicine, Chicago, Ill.* 134 pages. Charles C Thomas, Springfield, Ill., publishers, 1949. Price $3.50.

HISTOLOGY AND HISTOPATHOLOGY OF THE EYE AND ITS ADNEXA, by I. G. Sommers, M. D., *Assistant Professor (Ophthalmology), College Medical Evangelists; Medical Officer (E. E. N. T.), U. S. Public Health Service, Los Angeles, Calif.* 785 pages; illustrated. Grune & Stratton, New York, N. Y., publishers, 1949. Price $12.

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